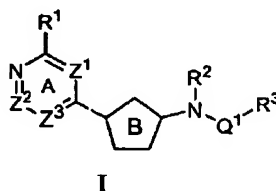


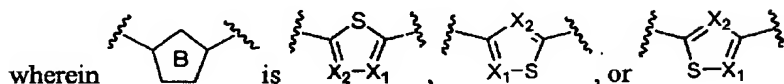
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AMENDMENTS TO THE CLAIMS

1. (Currently amended) A compound of formula I:



or a pharmaceutically acceptable salt thereof, wherein:



R^1 is halogen, CN, NO_2 , or V_mR ;

Z^1 and Z^3 are each independently CR^Z , and Z^2 is CR^1 ;

each occurrence of R^Z is independently halogen, CN, NO_2 , or U_nR' ;

R^2 is U_nR' ;

X^1 and X^2 are each independently CR^4 or N;

each occurrence of R^4 is independently halogen, CN, NO_2 , or V_mR ;

each occurrence of U or V is independently an optionally substituted C_{1-6} alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by $-NR-$, $-S-$, $-O-$, $-CS-$, $-CO_2-$, $-OCO-$, $-CO-$, $-COCO-$, $-CONR-$, $-NRCO-$, $-NRCO_2-$, $-SO_2NR-$, $-NRSO_2-$, $-CONRNR-$, $-NRCONR-$, $-OCONR-$, $-NRNR-$, $-NRSO_2NR-$, $-SO-$, or $-SO_2-$, $-P(O)-$, $-P(O)_2-$, or $-P(OR')-$;

m and n are each independently 0 or 1;

each occurrence of R is independently hydrogen or an optionally substituted C_{1-6} aliphatic group; and each occurrence of R' is independently hydrogen or an optionally substituted C_{1-6} aliphatic group, a 3-8-membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms

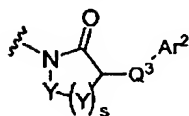
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independently selected from nitrogen, oxygen, or sulfur; or R and R', two occurrences of R, or two occurrences of R', are taken together with the atom(s) to which they are bound to form an optionally substituted 3-12 membered saturated, partially unsaturated, or fully unsaturated monocyclic or bicyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

Q¹ is -CO-, -SO₂-, or -SO₂NR-;

R³ is Q²-Ar¹,

or R² and Q¹-R³, taken together with the nitrogen atom, form the cyclic group:



, where s is 1 or 2, each occurrence of Y is independently, as valency and stability permit, -CO-, -CS-, -SO₂-, -O-, -S-, -NR⁵-, or -C(R⁵)₂-, and R⁵ is U_nR';

Q² and Q³ are each independently a bond or a C₁₋₆ alkylidene chain, wherein up to two methylene units of the chain are each optionally and independently replaced by -S-, -O-, -CS-, -CO₂-, -OCO-, -CO-, -COCO-, -CONR'-, -NR'CO-, -NR'CO₂-, -SO₂NR'-, -NR'SO₂-, -CONR'NR'-, -NR'CONR'-, -OCONR'-, -NR'NR'-, -NR'SO₂NR'-, -SO-, or -SO₂-, ~~P(O)-, P(O)₂-, or P(OR')-~~; and wherein any carbon atom in the one or more methylene units is optionally substituted with one or two occurrences of R⁶, wherein each occurrence of R⁶ is independently halogen, CN, NO₂, or U_nR', or two occurrences of R⁶, or R' and R⁶, taken together with the atoms to which they are bound, form an optionally substituted 3-6-membered cycloalkyl, heterocyclyl, aryl or heteroaryl ring; and

~~Ar¹ and Ar² are each independently,~~ is a 5-8 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from ~~nitrogen~~, oxygen[,] or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from ~~nitrogen~~, oxygen[,] or sulfur; wherein Ar¹ is and ~~Ar² are each~~ optionally substituted with 0-5 independent occurrences of TR⁷;

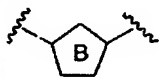
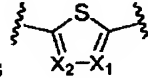
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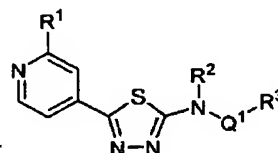
wherein T is a bond or is a C₁-C₆ alkylidene chain wherein up to two methylene units of T are optionally and independently replaced by -NR-, -S-, -O-, -CS-, -CO₂-, -OCO-, -CO-, -COCO-, -CONR-, -NRCO-, -NRCO₂-, -SO₂NR-, -NRSO₂-, -CONRNR-, -NRCONR-, -OCONR-, -NRNR-, -NRSO₂NR-, -SO-, or -SO₂-, P(O), P(O)₂, or P(OR¹);

Ar² is a 5-8 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein Ar² is optionally substituted with 0-5 independent occurrences of TR⁷; wherein T is a bond or is a C₁-C₆ alkylidene chain wherein up to two methylene units of T are optionally and independently replaced by -NR-, -S-, -O-, -CS-, -CO₂-, -OCO-, -CO-, -COCO-, -CONR-, -NRCO-, -NRCO₂-, -SO₂NR-, -NRSO₂-, -CONRNR-, -NRCONR-, -OCONR-, -NRNR-, -NRSO₂NR-, -SO-, or -SO₂-; and

each occurrence of R⁷ is independently R¹, halogen, NO₂, or CN;

provided that:

I) for compounds described where  is , one or more of, or all of the following conditions apply:



A) for compounds having the structure:

i) when R¹ is Cl, and R² is -CH(CH₃)COOCH₃ or hydrogen, then Q¹-R³ is not -CO(unsubstituted phenyl), -CO(unsubstituted 2-furyl), or -COCH₂(unsubstituted phenyl);

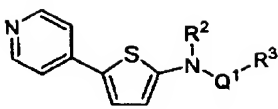
ii) when R¹ is hydrogen, R² is hydrogen, and Q¹ is -CO-, then R³ is not:

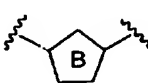
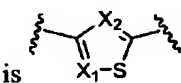
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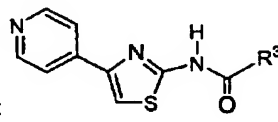
- a) phenyl substituted with 4-O(CH₂)₄₋₇CH₃ or 4-(CH₂)₄₋₇CH₃;
- b) phenyl substituted with 2-Cl, 4-NO₂, 4-Cl, 2-Br, 3-Br, 3-I, 3-CH₃, 4-OCH₃, 3-NO₂, or 4-I;
- c) 2,6-OCH₃-phenyl;
- d) (5-Cl, 3-CH₃, 1-F-phenyl)-pyrazol-4-yl; or
- e) 4-OnBu-phenyl, -CH₂O(2-F-phenyl), -(CH₂)₂phenyl, furan-2-yl, thiophen-2-yl, 4-CH₃-phenyl, -CH₂O(2-CH₃-phenyl), 3-OCH₃-phenyl, 2-(2,5-dimethoxyphenyl)quinolin-4-yl, -NH-(4-Cl-phenyl), -NH-(3,4-dichlorophenyl), (2-CO₂H, 3-NO₂)-phenyl, 3,5-dimethyl-1,2,4-oxazol-4-yl, -CH=CH-phenyl, 4-F-phenyl, C(CH₃)₂O-(4-Cl-phenyl), -NH(3-Cl-phenyl), -NHphenyl, unsubstituted phenyl, 3,4,5-OCH₃-phenyl, 4-NO₂-phenyl, 4-cyclopentoxo-phenyl, -(CH₂)₃phenyl, -(tricyclo[3.3.1.1^{3,7}]decan-1-yl, -CH₂O-(3-CH₃-phenyl), 3-NO₂-phenyl, -cyclopropyl-(4-tert-butyl-phenyl), 2,3-OCH₃-phenyl, 1,3-benzodioxo-5-yl, -CH₂-O-(4-F-phenyl), or 3-Br-phenyl;
- iii) when R¹ is hydrogen, R² is hydrogen, and Q¹ is -CSNH-, then R³ is not 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl;
- iv) when R¹ is hydrogen, R² is hydrogen, and Q¹ is SO₂, then R³ is not unsubstituted phenyl, unsubstituted benzyl, unsubstituted naphthyl, phenyl substituted with para-NHCOCH₃, para-NH₂, or para-CH₃; and
- v) when R¹ is hydrogen, R² is -CH₂CH=CH₂, and Q¹ is CO, then R³ is not 4-OCH₃-phenyl, unsubstituted naphthyl, -NH-(4-OCH₃-phenyl), 3,5-OCH₃-phenyl, -CH₂Ophenyl, -CH₂-thiophen-2-yl, or -CH(phenyl)(CH₂CH₃); and
- vi) when R¹ is hydrogen, R² is CH₂CH₃, and Q¹ is CO, then R³ is not 2,4-Cl-phenyl; and

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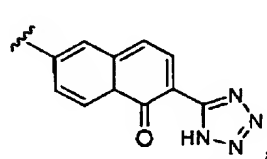
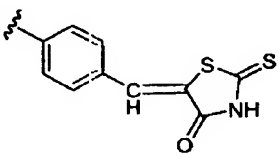
B) for compounds having the structure: , when R² is hydrogen or CH³, and Q¹ is -CO-, then R³ is not -OCH₂CH₂OCH₂phenyl;

II) for compounds described where  is , one or more of, or all of the following conditions apply:

A) for compounds having the structure: ,

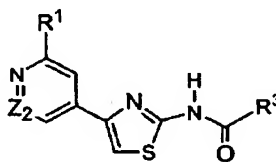
i) when R³ is Q²-Ar¹, and Q² is a bond then Ar¹ is not any one or more of the following: unsubstituted phenyl or phenyl substituted with 2-Br; 2-Cl; 2-I; 2,6-F; 3,5-OCH₃; 3,4,5-OCH₃; 2,4-OCH₃; 3,4-CH₃; 2,5-Cl; 3,4-OCH₃; 2-Cl; 5-NO₂; 3,5-Cl; 3-O(CH₂)₄CH₃; 3-O-n-butyl; 3-CF₃; 3-OCH₃; 3-Br; 3-NO₂; 3-CH₃; 3-O-phenyl; 3-Cl; 4-N(CH₃)₂; 4-N(CH₂CH₃)₂; 4-SO₂N(R')₂; 4-CN; 4-COOCH₃; 4-C(O)phenyl; 4-phenyl; 4-tert-butyl; 4-O-phenyl; 4-O-isopropyl; 4-OCH₃; 4-OCH₂CH₃; 4-O-n-butyl; 4-Cl; 4-Br; 4-F; 4-CH₃; 4-NO₂; 4-Cl; 3-NO₂; 4-morpholino; 3-NO₂; 2,5-dioxopyrrolidinyl, or 4-piperidinyl; and

ii) R³ is not any one or more of the following groups:

, , -CH=CH(thiophen-2-yl), -CH=CH-unsubstituted phenyl, -CH₂(3-NHCOPh-phenyl), -6-bromo-2-(4-ethylphenyl)-4-quinolinyl, -CH₂-pyrrolidine, unsubstituted cyclohexyl, unsubstituted benzyl, unsubstituted furan-2-yl, -CH=CH(3-NO₂-phenyl), -CH=CH(4-NO₂-phenyl), -CH₂-naphthyl, unsubstituted naphthyl, unsubstituted thiophene, unsubstituted cyclopropyl, 1,4-benzodioxin, 2-oxo-1-benzopyran, 4-oxo-1-benzopyran, 2-thienyl-quinolin-4-yl, 3-chloro-benzo[b]thiophen-2-yl,

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5-Br-(thiophen-2-yl), 5-Cl-(thiophen-2-yl), 5-NO₂-(thiophen-2-yl), 5-NO₂-(furan-2-yl), 2,5-Cl-(thiophen-3-yl), -CH=CH-(5-NO₂-thiophen-2-yl), 5-NO₂-(benzothiophen-2-yl), 3-OCH₃-(naphth-2-yl), -CH₂O(2,4-Cl-phenyl), -(CH₂)₂S-phenyl, 2-phenyl-quinolin-4-yl, -CH₂O(4-Cl-phenyl), -CH₂CH₂-3-(4-Cl-phenyl)-1-phenyl-1-H-pyrazol-4-yl, or -CH₂(1,3-dioxoisindole); and

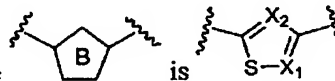


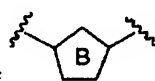
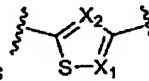
B) for compounds having the structure:

i) when R¹ is Cl, and X₁ is C-Cl, then R³ is not NHSO₂-(2-CF₃-phenyl) or -NHSO₂-(2,6-dimethoxy-phenyl);

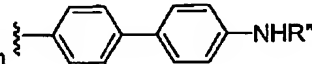
ii) when R¹ is CH₃, and X₁ is C-CH₃, then R³ is not an optionally substituted indole or optionally substituted dihydroindole; and

C) for compounds of general formula I, when Z₁, Z₂ and Z₃ are each CH, R¹ is H, X¹ is CH and X₂ is C-COOCH₃, then R³ is not 2-(4-ethyl-phenyl)-6-bromo-quinolin-4-yl; and



III) for compounds described above where  is , one or more of, or all of the following conditions apply:

A) when Z¹, Z² and Z³ are each CH, X² is N, X¹ is CH, Q¹ is -CONR-, and R² is hydrogen or -CH₃, then R³ is not optionally substituted pyridyl, optionally substituted thiazol-4-yl, -CH₂pyridyl, benzimidazol-4-yl, quinolin-2-yl, 1-bromo-isoquinolin-3-yl, benzthiazol-2-yl, optionally substituted 5,6,7,8-tetrahydronaphthyridin-2-yl, or phenyl substituted with -CH₂piperidinyl; and

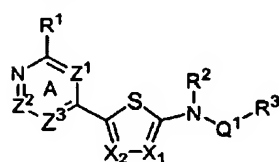
B) when Z¹, Z² and Z³ are each CH, X² is N, X¹ is CH, Q¹ is SO₂, and R² is hydrogen, then R³ is not phenyl substituted with  where R'' is hydrogen or -COCH₃;

C) when Z¹, Z² and Z³ are each CH, X₁ is C-CO₂H, X² is CH, R² is hydrogen, and Q¹ is SO₂, then R³ is not 2-CH₃-phenyl; and

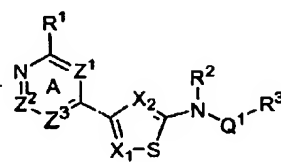
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D) when Z^1 , Z^2 and Z^3 are each CH, X_1 is CH, X^2 is N, R^2 is hydrogen, and Q^1 is CO, then R^3 is not 5-methoxy-6-trifluoromethyl-1H-indole.

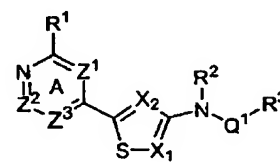
2. (Original) The compound of claim 1, wherein the compound has one of the structures:



I-A

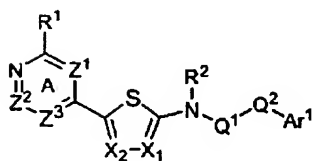


I-B

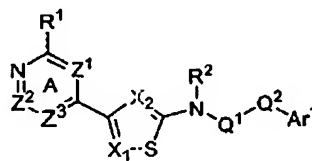


or I-C.

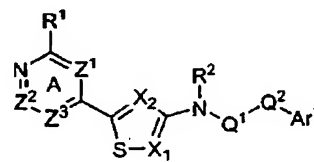
3. (Original) The compound of claim 1, wherein R^3 is Q^2-Ar^1 and compounds have one of formulas I-A-i, I-B-i, or I-C-i:



I-A-i



I-B-i



I-C-i.

4. (Original) The compound of claim 3, wherein R^2 is hydrogen, or is U_nR^2 , where n is 1, and U is a C_{1-6} alkylidene chain wherein one or two methylene units are optionally and independently replaced by O, NR, S, or C(O).

5. (Original) The compound of claim 3, wherein U is $-CH_2-$, $-CH_2CH_2-$, $-CH_2CH_2CH_2-$, $-CH_2CH_2CH_2CH_2-$, $-CH_2O-$, $-CH_2S-$, $-CH_2NR-$, $-CH_2CH_2O-$, $-CH_2CH_2S-$, $-CH_2CH_2NR-$, $-CH_2CH_2CH_2O-$, $-CH_2CH_2CH_2S-$, $-CH_2CH_2CH_2NR-$, $-CH_2CH_2CH_2CH_2O-$, $-CH_2CH_2CH_2CH_2S-$, $-CH_2CH_2CH_2CH_2NR-$, $-CH_2CH_2OCH_2CH_2-$, $-(CH_2)_4NHCH_2-$, $-(CH_2)_3NHCH_2CH_2-$, or

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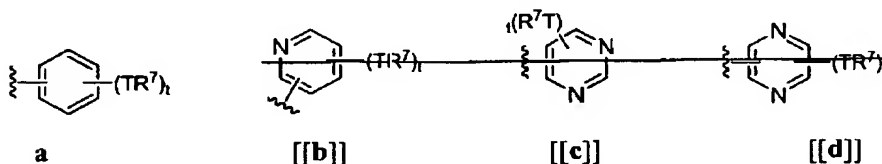
-CH₂CH₂NHCH₂CH₂-, and preferred R' groups are hydrogen, C₁-C₄alkyl, optionally substituted tetrahydropyranyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, pyridinyl, phenyl, or cyclohexyl, or R and R', taken together with the nitrogen atom to which they are bound, form an optionally substituted 5- or 6-membered heterocyclyl ring.

6. (Original) The compound of claim 3, wherein Q¹ is -C(O)- or -SO₂NR-.

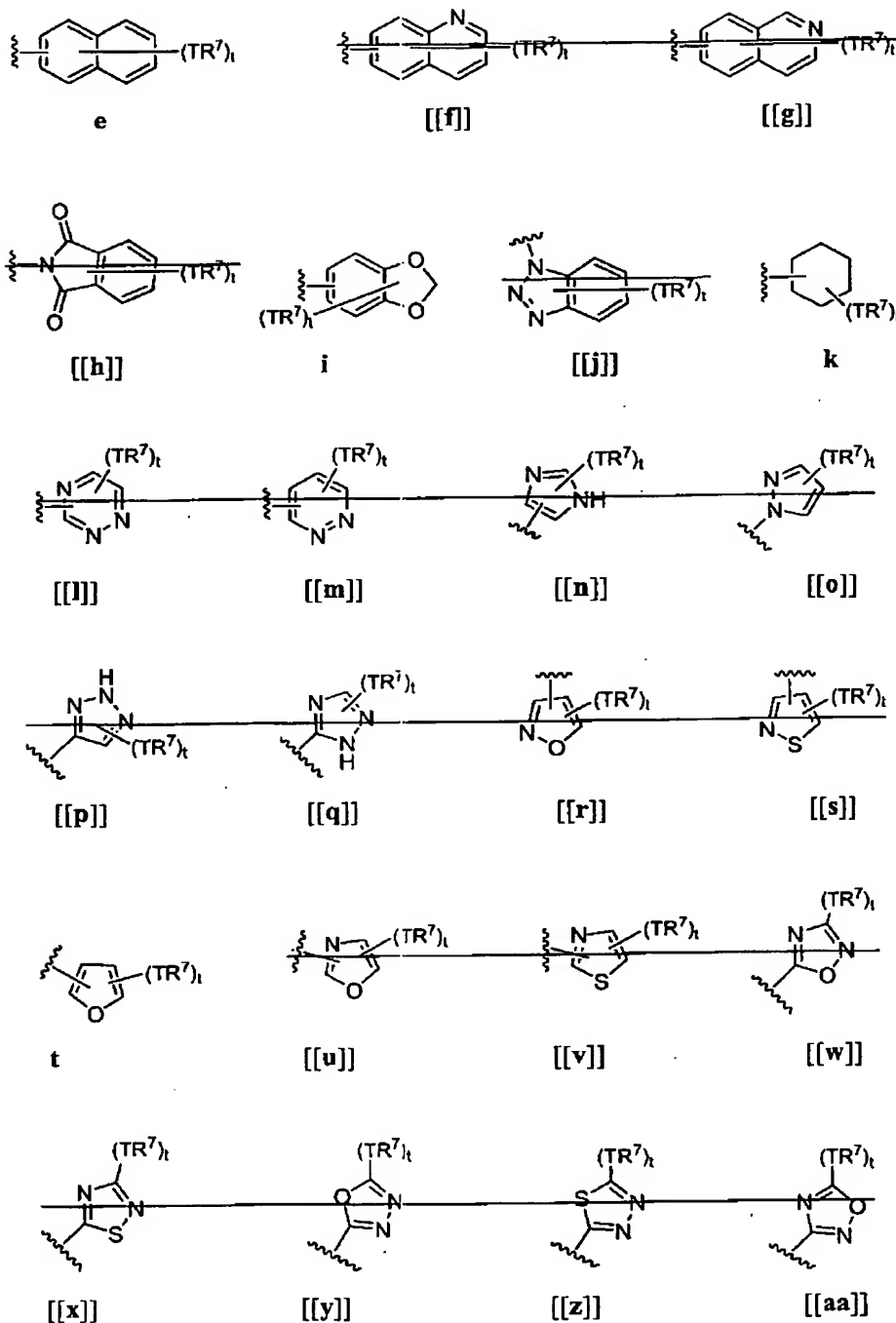
7. (Original) The compound of claim 3, wherein Q² is a direct bond, or is -(CHR⁶)_q-, -(CHR⁶)_qO-, -(CHR⁶)_qS-, -(CHR⁶)_qS(O)₂-, -(CHR⁶)_qS(O)-, -(CHR⁶)_qNR-, or -(CHR⁶)_qC(O)-, wherein q is 0, 1, 2, or 3, and R⁶ is R', -N(R)(R'), -(CH₂)₁₋₄N(R)(R'), -OR', -(CH₂)₁₋₄OR', -NR(CH₂)₁₋₄N(R)(R'), -NR(CH₂)₁₋₄SO₂R', -NR(CH₂)₁₋₄COOR', or -NR(CH₂)₁₋₄COR', or two occurrences of R⁶, taken together with the atoms to which they are bound, form an optionally substituted 3-6-membered saturated, partially unsaturated, or fully unsaturated ring.

8. (Original) The compound of claim 7, wherein R⁶ is CH₂OH, CH₂CH₂OH, OH, OMe, OEt, NH₂, NH(Me), NH(Et), N(Me)(Me), CH₂NH₂, CH₂CH₂NH₂, NHCO₂*t*-butyl, phenyl, cyclopentyl, methyl, ethyl, isopropyl, cyclopropyl, NH(CH₂)₃NH₂, NH(CH₂)₂NH₂, NH(CH₂)₂NHEt, NHCH₂pyridyl, NHSO₂phenyl, NHC(O)CH₂C(O)O*t*-butyl, NHC(O)CH₂NH₃, and NHCH₂-imidazol-4-yl.

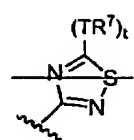
9. (Currently amended) The compound of claim 3, wherein Ar¹ is:



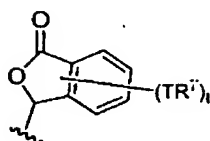
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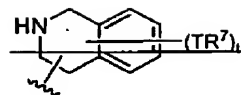
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[[bb]]



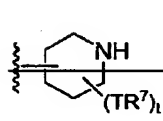
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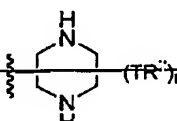
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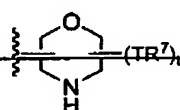
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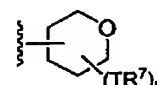
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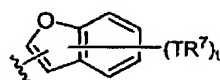
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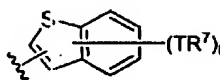
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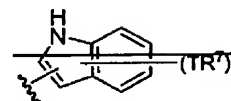
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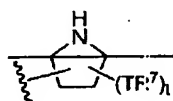
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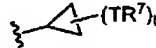
[[ll]]



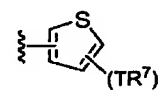
mm



[[nn]]



oo



pp

wherein t is 0, 1, 2, 3, 4 or 5, and wherein any Ar^1 is bonded to Q^2 through any substitutable ~~nitrogen~~ or carbon atom, and wherein one or more hydrogen atoms on any substitutable ~~nitrogen~~ or carbon atom is substituted with one or more independent occurrences of TR^7 .

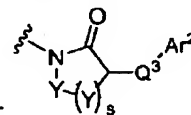
10. (Currently amended) The compound of claim 9, wherein Ar^1 is a, [[b,]] e, [[g,]] [[b,]] i, [[j,]] k, [[r,]] cc, [[dd,]] [[ff,]] jj, [[ll,]] or pp.

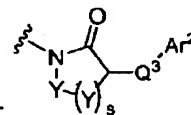
Applicants: Jingrong Cao et al.
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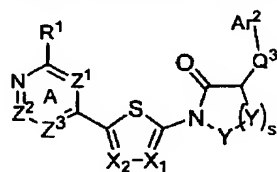
11. (Original) The compound of claim 9, wherein T is a bond or is an optionally substituted C_{1-6} alkylidene chain wherein one or two methylene units are optionally and independently replaced by -O-, -NR-, -S-, -SO₂-, -COO-, -CO-, -OSO₂-, -NRSO₂-, -CONR-, or -SO₂NR-, and R⁷ is R' or halogen.

12. (Original) The compound of claim 9, wherein each occurrence of TR⁷ is independently -C₁₋₃alkyl, -OR', -SR', -CF₃, -OCF₃, -SCF₃, -F, -Cl, I, -Br, -COOR', -COR', -O(CH₂)₄N(R)(R'), -O(CH₂)₃N(R)(R'), -O(CH₂)₂N(R)(R'), -O(CH₂)N(R)(R'), -O(CH₂)₄CON(R)(R'), -O(CH₂)₃CON(R)(R'), -O(CH₂)₂CON(R)(R'), -O(CH₂)CON(R)(R'), -C(O)N(R)(R'), -(CH₂)₄OR', -(CH₂)₃OR', -(CH₂)₂OR', -CH₂OR', optionally substituted phenyl or benzyl, -N(R)(R'), -(CH₂)₄N(R)(R'), -(CH₂)₃N(R)(R'), -(CH₂)₂N(R)(R'), -(CH₂)N(R)(R'), or SO₂N(R)(R'), NRSO₂R', CON(R)(R'), or -OSO₂R'.

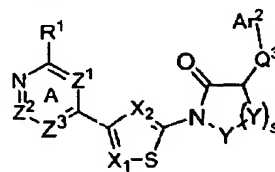
13. (Original) The compound of claim 1, wherein R³ is Q²-Ar¹, or R² and Q¹-R³,



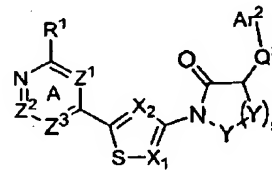
taken together with the nitrogen atom, form the cyclic group: , where s is 1 or 2, each occurrence of Y is independently, as valency and stability permit, -CO-, -CS-, -SO₂-, -O-, -S-, -NR⁵-, or -C(R⁵)₂-, and R⁵ is U_nR', and compounds of formula I-A-ii, I-B-ii, and I-C-ii are provided:



I-A-ii



I-B-ii



I-C-ii.

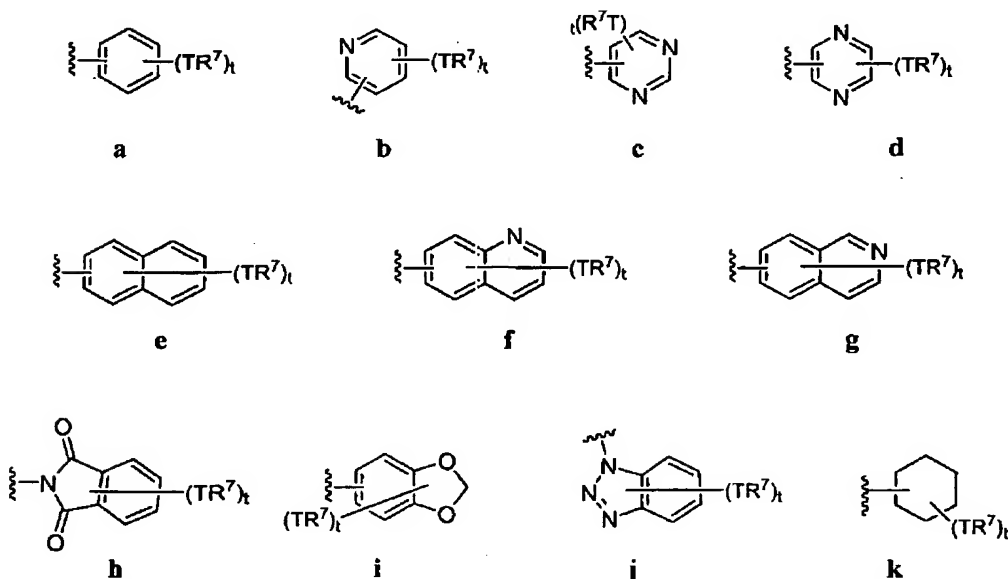
14. (Original) The compound of claim 13, wherein Q³ is a direct bond, or is

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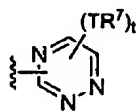
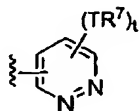
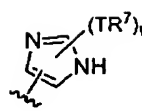
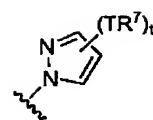
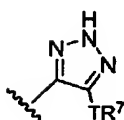
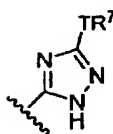
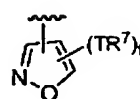
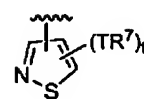
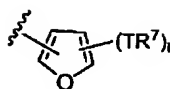
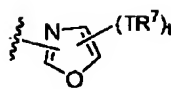
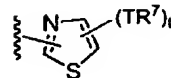
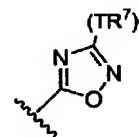
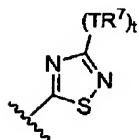
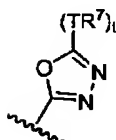
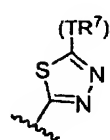
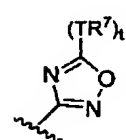
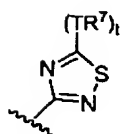
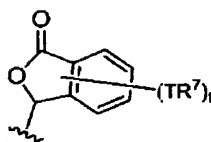
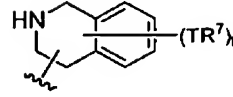
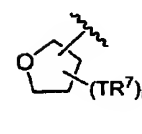
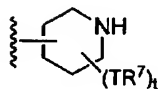
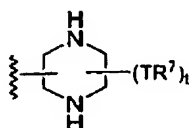
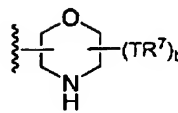
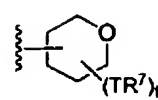
$-(\text{CHR}^6)_q-$, $-(\text{CHR}^6)_q\text{O}-$, $-(\text{CHR}^6)_q\text{S}-$, $-(\text{CHR}^6)_q\text{S}(\text{O})_2-$, $-(\text{CHR}^6)_q\text{S}(\text{O})-$, $-(\text{CHR}^6)_q\text{NR}-$,
 or $-(\text{CHR}^6)_q\text{C}(\text{O})-$, wherein q is 0, 1, 2, or 3, and R^6 is R' , $-\text{N}(\text{R})(\text{R}')$,
 $-(\text{CH}_2)_{1-4}\text{N}(\text{R})(\text{R}')$, $-\text{OR}'$, $-(\text{CH}_2)_{1-4}\text{OR}'$, $-\text{NR}(\text{CH}_2)_{1-4}\text{N}(\text{R})(\text{R}')$, $-\text{NR}(\text{CH}_2)_{1-4}\text{SO}_2\text{R}'$,
 $-\text{NR}(\text{CH}_2)_{1-4}\text{COOR}'$, or $-\text{NR}(\text{CH}_2)_{1-4}\text{COR}'$, or two occurrences of R^6 , taken together
 with the atoms to which they are bound, form an optionally substituted 3-6-membered
 saturated, partially unsaturated, or fully unsaturated ring.

15. (Original) The compound of claim 14, wherein R^6 is CH_2OH , $\text{CH}_2\text{CH}_2\text{OH}$,
 OH , OMe , OEt , NH_2 , $\text{NH}(\text{Me})$, $\text{NH}(\text{Et})$, $\text{N}(\text{Me})(\text{Me})$, CH_2NH_2 , $\text{CH}_2\text{CH}_2\text{NH}_2$,
 $\text{NHCO}_2t\text{-butyl}$, phenyl, cyclopentyl, methyl, ethyl, isopropyl, cyclopropyl,
 $\text{NH}(\text{CH}_2)_3\text{NH}_2$, $\text{NH}(\text{CH}_2)_2\text{NH}_2$, $\text{NH}(\text{CH}_2)_2\text{NHEt}$, $\text{NHCH}_2\text{pyridyl}$, $\text{NHSO}_2\text{phenyl}$,
 $\text{NHC}(\text{O})\text{CH}_2\text{C}(\text{O})\text{O}t\text{-butyl}$, $\text{NHC}(\text{O})\text{CH}_2\text{NH}_3$, and $\text{NHCH}_2\text{-imidazol-4-yl}$.

16. (Original) The compound of claim 13, wherein Ar^2 is:

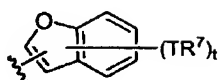


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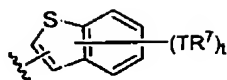
**l****m****n****o****p****q****r****s****t****u****v****w****x****y****z****aa****bb****cc****dd****ee****ff****gg****hh****ii**

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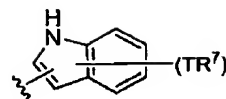
Application No.: 10/696,862



jj



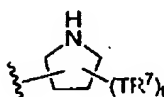
kk



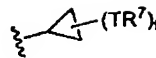
ll



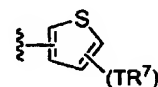
mm



nn



oo



pp

wherein t is 0, 1, 2, 3, 4 or 5, and wherein any Ar^2 is bonded to Q^3 through any substitutable nitrogen or carbon atom, and wherein one or more hydrogen atoms on any substitutable nitrogen or carbon atom is substituted with one or more independent occurrences of TR^7 .

17. (Original) The compound of claim 16, wherein Ar^2 is a, b, c, g, h, i, j, k, n, r, cc, dd, ff, jj, ll, or pp.

18. (Original) The compound of claim 16, wherein T is a bond or is an optionally substituted C_{1-6} alkylidene chain wherein one or two methylene units are optionally and independently replaced by -O-, -NR-, -S-, -SO₂-, -COO-, -CO-, -OSO₂-, -NRSO₂-, -CONR-, or -SO₂NR-, and R^7 is R' or halogen.

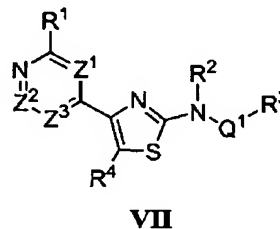
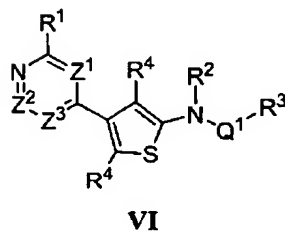
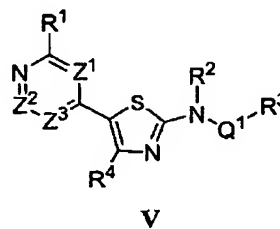
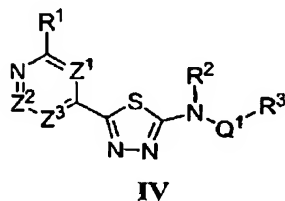
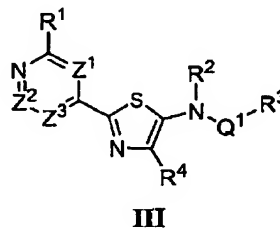
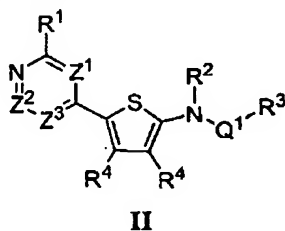
19. (Original) The compound of claim 16, wherein each occurrence of TR^7 is independently -C₁₋₃alkyl-, -OR', -SR', -CF₃-, -OCF₃-, -SCF₃-, -F-, -Cl-, I-, -Br-, -COOR', -COR', -O(CH₂)₄N(R)(R'), -O(CH₂)₃N(R)(R'), -O(CH₂)₂N(R)(R'), -O(CH₂)N(R)(R'), -O(CH₂)₄CON(R)(R'), -O(CH₂)₃CON(R)(R'), -O(CH₂)₂CON(R)(R'), -O(CH₂)CON(R)(R'), -C(O)N(R)(R'), -(CH₂)₄OR', -(CH₂)₃OR', -(CH₂)₂OR', -CH₂OR', optionally substituted phenyl or benzyl, -N(R)(R'), -(CH₂)₄N(R)(R'),

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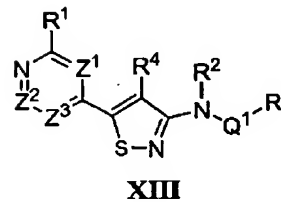
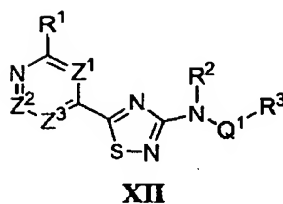
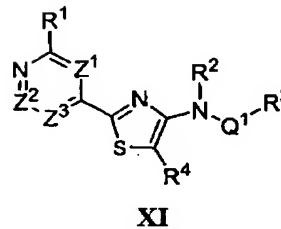
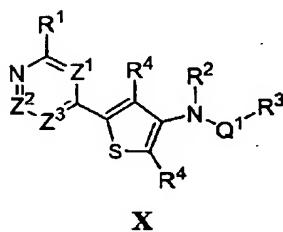
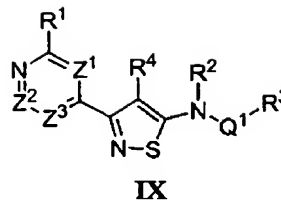
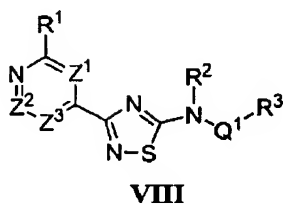
$-(\text{CH}_2)_3\text{N}(\text{R})(\text{R}')$, $-(\text{CH}_2)_2\text{N}(\text{R})(\text{R}')$, $-(\text{CH}_2)\text{N}(\text{R})(\text{R}')$, or $\text{SO}_2\text{N}(\text{R})(\text{R}')$, $\text{NRSO}_2\text{R}'$, $\text{CON}(\text{R})(\text{R}')$, or $-\text{OSO}_2\text{R}'$.

20. (Original) The compound of claim 13, wherein R^5 is hydrogen, $(\text{CH}_2)_3\text{OR}'$, $(\text{CH}_2)_2\text{OR}'$, $(\text{CH}_2)\text{OR}'$, $(\text{CH}_2)_3\text{N}(\text{R}')_2$, $(\text{CH}_2)_2\text{N}(\text{R}')_2$, $(\text{CH}_2)\text{N}(\text{R}')_2$, or $\text{C}_{1-4}\text{aliphatic}$.

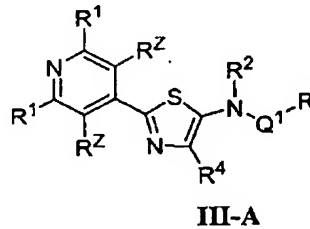
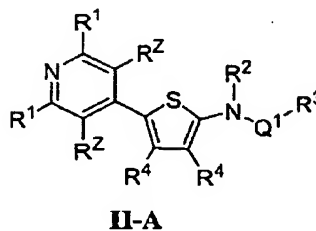
21. (Original) The compound of claim 1, wherein X^1 and X^2 are each independently CR^4 or N , and compounds have one of formulas II, III, IV, V, VI, VII, VIII, IX, X, XI, XII, or XIII:



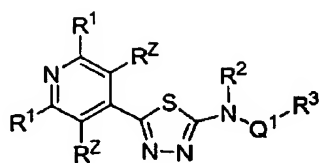
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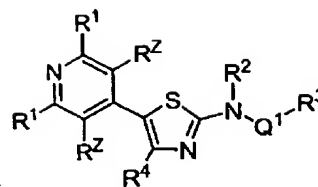
22. (Previously presented) The compound of claim 21, wherein compounds have one of formulas II-A, III-A, IV-A, V-A, VI-A, VII-A, VIII-A, IX-A, X-A, XI-A, XII-A, or XIII:



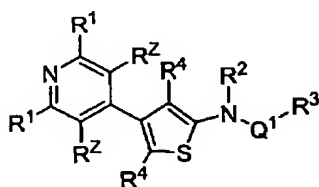
Applicants: Jingrong Cao et al.
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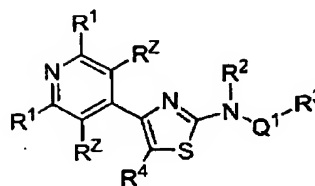
IV-A



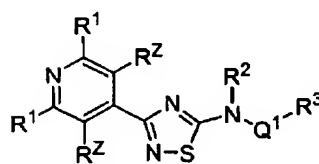
V-A



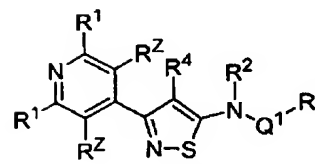
VI-A



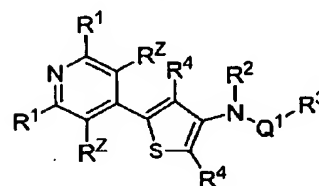
VII-A



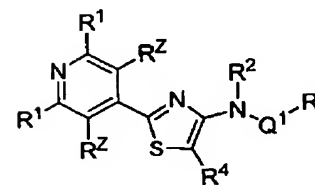
VIII-A



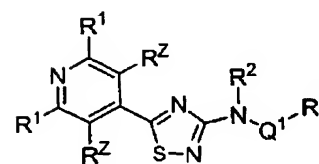
IX-A



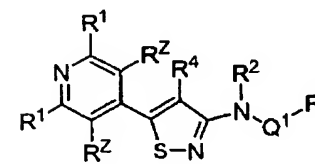
X-A



XI-A



XII-A

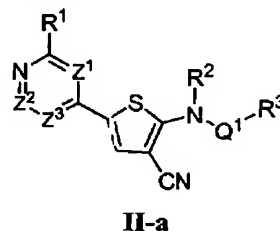


XIII-A

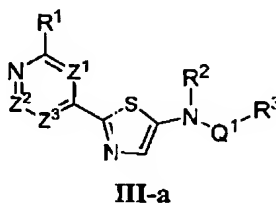
23. (Original) The compound of claim 1, wherein each occurrence of R^1 is independently hydrogen, halogen, optionally substituted C_1 - C_4 aliphatic, OR, SR, or $N(R)_2$.

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24. (Currently amended) The compound of claim 23, wherein each occurrence of R^1 is independently hydrogen, halogen, $-CH_3$, $-CH_2CH_3$, $-OH$, $-OCH_3$, $-SCH_3$, $-NH_2$, $-N(CH_3)_2$, $-N(CH_2CH_3)_2$, $-NH(CH_2)_2NHCH_3$, $-NH(cyclopropyl)$, $-NH(CH_2)cyclopropyl$, or $-NH(CH_2)_2N(CH_3)_2$.
25. (Original) The compound of claim 1, wherein each occurrence of R^Z is independently hydrogen, halogen, C_1 - C_4 aliphatic, OH , OR' , or $N(R)(R')$.
26. (Original) The compound of claim 25, wherein each occurrence of R^Z is independently hydrogen, halogen, Me , OH , OMe , NH_2 , or $N(Me)_2$.
27. (Original) The compound of claim 1, wherein R^4 groups are each independently hydrogen, C_1 - C_4 aliphatic, CN , COR , $C(=O)OR$, $C(=O)N(R)_2$, or halogen.
28. (Original) The compound of claim 1, wherein one occurrence of R^4 is CN and compounds have the general structure II-a:

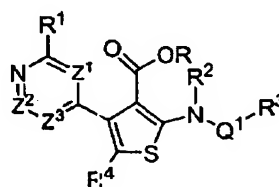


29. (Original) The compound of claim 1, wherein R^4 is hydrogen and compounds have the general structure III-a:



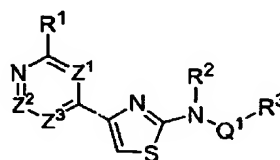
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30. (Original) The compound of claim 1, wherein one occurrence of R^4 is hydrogen and the other occurrence of R^4 is $-COOR$ and compounds have the general structure VI-a:



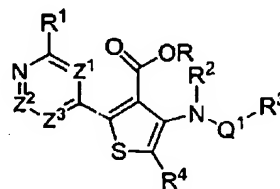
VI-a

31. (Original) The compound of claim 1, wherein R^4 is hydrogen and compounds have the general structure VII-a:



VII-a

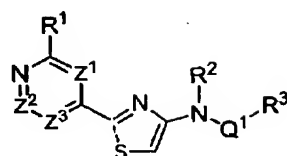
32. (Original) The compound of claim 1, wherein one occurrence of R^4 is hydrogen and the other occurrence of R^4 is $C(=O)OR$ and compounds have the general structure X-a:



X-a

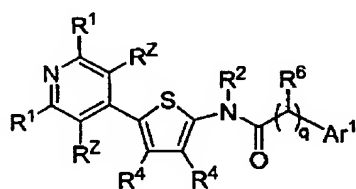
33. (Original) The compound of claim 1, wherein R^4 is hydrogen and compounds have the general structure XI-a:

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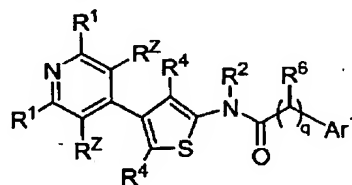


XI-a

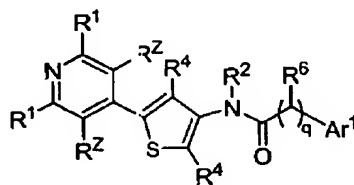
34. (Currently amended) The compound of claim 2 [[1]], wherein Q^1 is $-CO-$, Q^2 is CHR^6 , q is 1, 2, or 3, and compounds have one of formulas XIV, XV, or XVI:



XIV

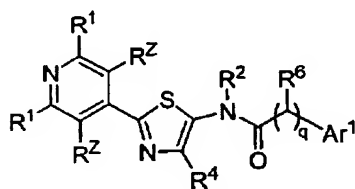


XV

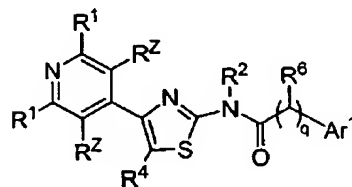


XVI

35. (Currently amended) The compound of claim 2 [[1]], wherein Q^1 is $-CO-$, Q^2 is CHR^6 , q is 1, 2 or 3, and compounds have one of formulas XVII, XVIII, or XIX:

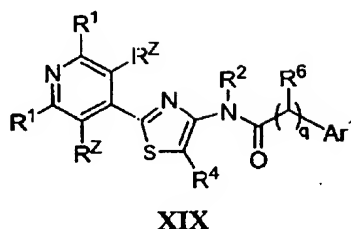


XVII



XVIII

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36. (Currently amended) The compound of claims 34 or 35, wherein compound variables are selected from one or more of the following groups:

- a) each occurrence of R^1 is independently hydrogen, halogen, optionally substituted C_1 - C_4 aliphatic, OR, SR, or $N(R)_2$;
- b) each occurrence of R^1 is independently hydrogen, halogen, $-CH_3$, $-CH_2CH_3$, $-OH$, $-OCH_3$, $-SCH_3$, $-NH_2$, $-N(CH_3)_2$, $-N(CH_2CH_3)_2$, $-NH(CH_2)_2NHCH_3$, $-NH(cyclopropyl)$, $-NH(CH_2)cyclopropyl$, or $-NH(CH_2)_2N(CH_3)_2$;
- c) each occurrence of R^Z is independently hydrogen, halogen, optionally substituted C_1 - C_4 aliphatic, OH, $O(R')$, or $N(R)(R')$;
- d) each occurrence of R^Z is independently hydrogen, halogen, Me, OH, OMe, NH_2 , or $N(Me)_2$;
- e) R^2 is hydrogen, or is U_nR' , where n is 1, and U is $-CH_2-$, $-CH_2CH_2-$, $-CH_2CH_2CH_2-$, $-CH_2CH_2CH_2CH_2-$, $-CH_2O-$, $-CH_2S-$, $-CH_2NR-$, $-CH_2CH_2O-$, $-CH_2CH_2S-$, $-CH_2CH_2NR-$, $-CH_2CH_2CH_2O-$, $-CH_2CH_2CH_2S-$, $-CH_2CH_2CH_2NR-$, $-CH_2CH_2CH_2CH_2O-$, $-CH_2CH_2CH_2CH_2S-$, $-CH_2CH_2CH_2CH_2NR-$, $-CH_2CH_2OCH_2CH_2-$, $-(CH_2)_4NHCH_2-$, $-(CH_2)_3NHCH_2CH_2-$, or $-CH_2CH_2NHCH_2CH_2-$, and R' groups are hydrogen, C_1 - C_4 alkyl, optionally substituted tetrahydropyranyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, pyridinyl, phenyl, or cyclohexyl, or R and R' , taken together with the nitrogen atom to which they are bound, form an optionally substituted 5- or 6-membered heterocycl ring;
- f) each occurrence of R^4 is independently hydrogen, C_1 - C_4 aliphatic, CN, COR, COOR, $CON(R)_2$, or halogen;

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g) q is 1, 2, or 3;

h) R^6 is R' , $-N(R)(R')$, $-(CH_2)_{1-4}N(R)(R')$, $-OR'$, $-(CH_2)_{1-4}OR'$, $-NR(CH_2)_{1-4}N(R)(R')$, $-NR(CH_2)_{1-4}SO_2R'$, $-NR(CH_2)_{1-4}COOR'$, or $-NR(CH_2)_{1-4}COR'$, or two occurrences of R^6 , taken together with the atoms to which they are bound, form an optionally substituted 3-6-membered saturated, partially unsaturated, or fully unsaturated ring;

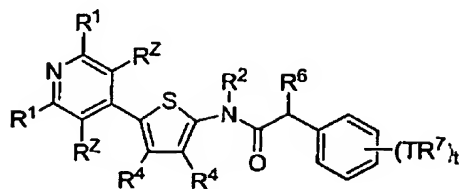
i) R^6 is CH_2OH , CH_2CH_2OH , OH , OMe , OEt , NH_2 , $NH(Me)$, $NH(Et)$, $N(Me)(Me)$, CH_2NH_2 , $CH_2CH_2NH_2$, $NHCO_2t\text{-butyl}$, phenyl, cyclopentyl, methyl, ethyl, isopropyl, cyclopropyl, $NH(CH_2)_3NH_2$, $NH(CH_2)_2NH_2$, $NH(CH_2)_2NHEt$, $NHCH_2\text{pyridyl}$, $NHSO_2\text{phenyl}$, $NHC(C)CH_2C(O)Ot\text{-butyl}$, $NHC(O)CH_2NH_3$, and $NHCH_2\text{-imidazol-4-yl}$;

j) Ar^1 is ring a, $[[b,]]$ e, $[[g,]]$ $[[h,]]$ i, $[[j,]]$ k, $[[r,]]$ cc, $[[dd,]]$ $[[ff,]]$ jj, $[[ll,]]$ or pp wherein t is 0, 1, 2, or 3, and T is a bond or is an optionally substituted C_{1-6} alkylidene chain wherein one or two methylene units are optionally and independently replaced by $-O-$, $-NR-$, $-S-$, $-SO_2-$, $-COO-$, $-CO-$, $-OSO_2-$, $-NRSO_2-$, $-CONR-$, or $-SO_2NR-$, and R^7 is R' or halogen; or

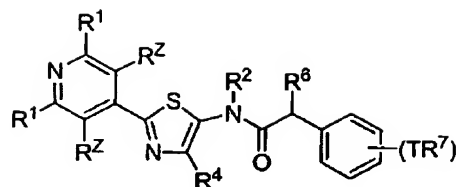
k) Ar^1 is ring a; $[[b,]]$ e, $[[g,]]$ $[[h,]]$ i, $[[j,]]$ k, $[[r,]]$ cc, $[[dd,]]$ $[[ff,]]$ jj, $[[ll,]]$ or pp wherein t is 0, 1, 2, or 3, and each occurrence of TR^7 is independently $-C_{1-3}\text{alkyl}$, $-OR'$, $-SR'$, $-CF_3$, $-OCF_3$, $-SCF_3$, $-F$, $-Cl$, I , $-Br$, $-COOR'$, $-COR'$, $-O(CH_2)_4N(R)(R')$, $-O(CH_2)_3N(R)(R')$, $-O(CH_2)_2N(R)(R')$, $-O(CH_2)N(R)(R')$, $-O(CH_2)_4CON(R)(R')$, $-O(CH_2)_3CON(R)(R')$, $-O(CH_2)_2CON(R)(R')$, $-O(CH_2)CON(R)(R')$, $-C(O)N(R)(R')$, $-(CH_2)_4OR'$, $-(CH_2)_3OR'$, $-(CH_2)_2OR'$, $-CH_2OR'$, optionally substituted phenyl or benzyl, $-N(R)(R')$, $-(CH_2)_4N(R)(R')$, $-(CH_2)_3N(R)(R')$, $-(CH_2)_2N(R)(R')$, $-(CH_2)N(R)(R')$, $[[or]]$ $-SO_2N(R)(R')$, $-NRSO_2R'$, $-CON(R)(R')$, or $-OSO_2R'$

37. (Currently amended) The compound of claim 34 or 35, q is 1, and Ar^1 is optionally substituted phenyl and compounds of general formula XIV-A through XIX-A are provided:

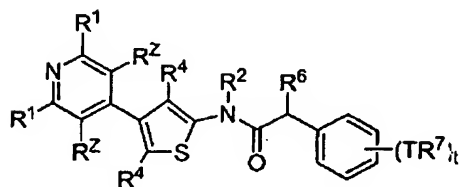
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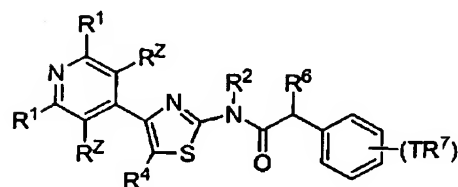
XIV-A



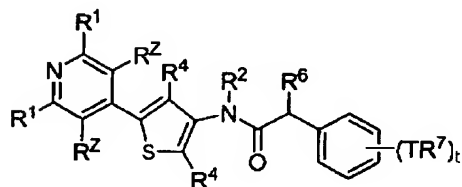
XV-A



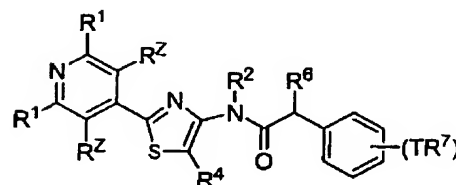
XVI-A



XVII-A



XVIII-A



XIX-A

wherein:

each occurrence of R^1 is hydrogen;

each occurrence of R^2 is hydrogen;

R^2 is hydrogen, or is U_nR' , where n is 1, and U is $-CH_2-$, $-CH_2CH_2-$,

$-CH_2CH_2CH_2-$, $-CH_2CH_2CH_2CH_2-$, $-CH_2O-$, $-CH_2S-$, $-CH_2NR-$, $-CH_2CH_2O-$,

$-CH_2CH_2S-$, $-CH_2CH_2NR-$, $-CH_2CH_2CH_2O-$, $-CH_2CH_2CH_2S-$, $-CH_2CH_2CH_2NR-$,

$-CH_2CH_2CH_2CH_2O-$, $-CH_2CH_2CH_2CH_2S-$, $-CH_2CH_2CH_2CH_2NR-$,

$-CH_2CH_2OCH_2CH_2-$, $-(CH_2)_4NHCH_2-$, $-(CH_2)_3NHCH_2CH_2-$, or

$-CH_2CH_2NHCH_2CH_2-$, and R' groups are hydrogen, C_1 - C_4 alkyl, optionally substituted tetrahydropyranyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl,

thiomorpholinyl, pyridinyl, phenyl, or cyclohexyl, or R and R' , taken together with the

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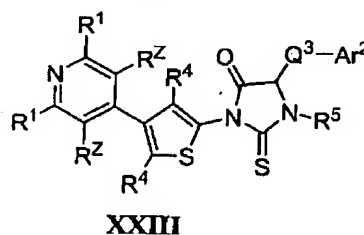
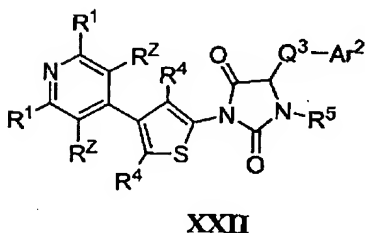
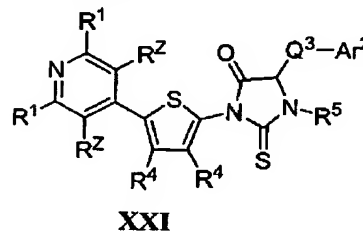
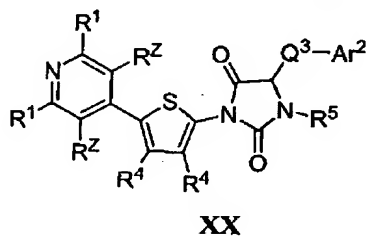
nitrogen atom to which they are bound, form an optionally substituted 5- or 6-membered heterocyclyl ring;

each occurrence of R^4 is independently hydrogen, C_{1-6} aliphatic, CN, COR, COOR, $CON(R)_2$, or halogen;

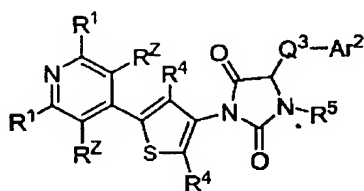
R^6 is R' , $-N(R)(R')$, $-(CH_2)_{1-4}N(R)(R')$, $-OR'$, $-(CH_2)_{1-4}OR'$, $-NR(CH_2)_{1-4}N(R)(R')$, $-NR(CH_2)_{1-4}SO_2R'$, $-NR(CH_2)_{1-4}COOR'$, or $-NR(CH_2)_{1-4}COR'$; and

t is 0, 1, 2, or 3, and each occurrence of TR^7 is independently $-C_{1-3}$ alkyl, $-OR'$, $-SR'$, $-CF_3$, $-OCF_3$, $-SCF_3$, $-F$, $-Cl$, I , $-Br$, $-COOR'$, $-COR'$, $-O(CH_2)_4N(R)(R')$, $-O(CH_2)_3N(R)(R')$, $-O(CH_2)_2N(R)(R')$, $-O(CH_2)N(R)(R')$, $-O(CH_2)_4CON(R)(R')$, $-O(CH_2)_3CON(R)(R')$, $-O(CH_2)_2CON(R)(R')$, $-O(CH_2)CON(R)(R')$, $-C(O)N(R)(R')$, $-(CH_2)_4OR'$, $-(CH_2)_3OR'$, $-(CH_2)_2OR'$, $-CH_2OR'$, optionally substituted phenyl or benzyl, $-N(R)(R')$, $-(CH_2)_4N(R)(R')$, $-(CH_2)_3N(R)(R')$, $-(CH_2)_2N(R)(R')$, $-(CH_2)N(R)(R')$, $[[or]] -SO_2N(R)(R')$, $-NRSO_2R'$, $-CON(R)(R')$, or $-OSO_2R'$.

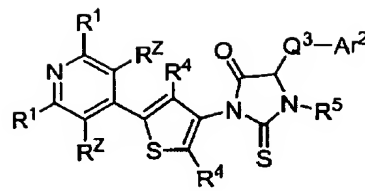
38. (Currently amended) The compound of claim 16 [[1]], wherein R^2 and Q^1-R^3 , taken together with the atoms to which they are bound form a 5-membered cyclic group, and compounds have the general formula XX through XXV:



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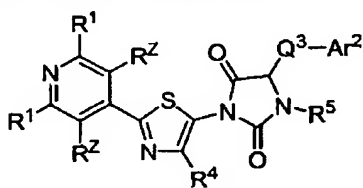


XXIV

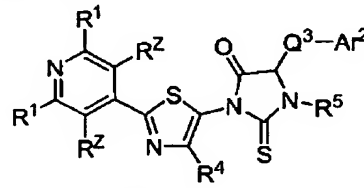


XXV

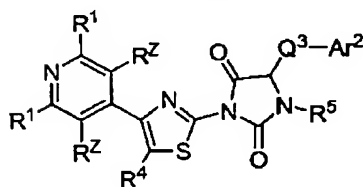
39. (Currently amended) The compound of claim 16 [[1]], R² and Q¹-R³, taken together with the atoms to which they are bound form a 5-membered cyclic group, and compounds have the general formula XXVI through XXXI:



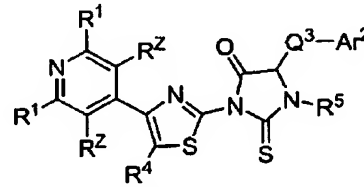
XXVI



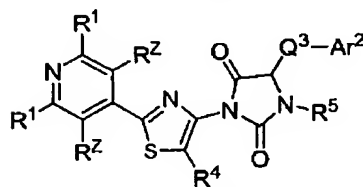
XXVII



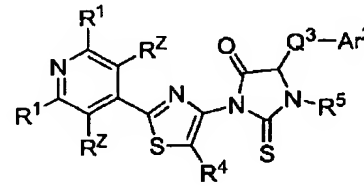
XXVIII



XXIX



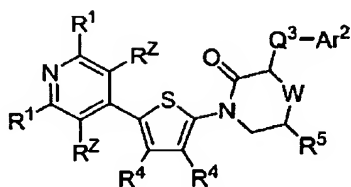
XXX



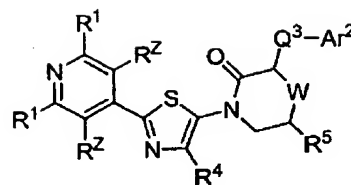
XXXI

40. (Currently amended) The compound of claim 16 [[1]], wherein R² and Q¹-R³, taken together with the atoms to which they are bound form a 6-membered cyclic group, and compounds have the general formula XXXII through XXXVII:

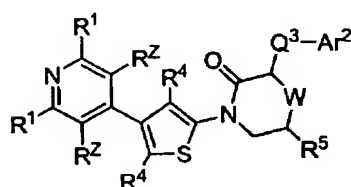
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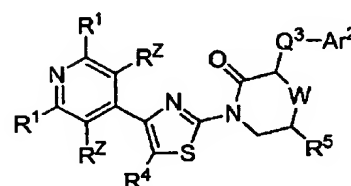
XXXII



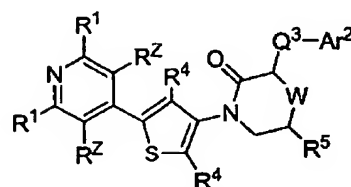
XXXIII



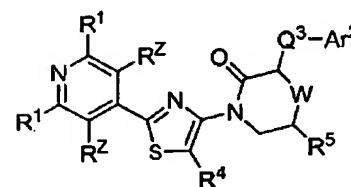
XXXIV



XXXV



XXXVI



XXXVII

wherein W is O, NR⁵, or CHR⁵.

41. (Original) The compound of claims 38, 39 or 40, wherein compound variables are selected from one of more of the following groups:

- a) each occurrence of R¹ is independently hydrogen, halogen, optionally substituted C₁-C₄aliphatic, OR, SR, or N(R)₂;
- b) each occurrence of R² is independently hydrogen, halogen, optionally substituted C₁-C₄aliphatic, OH, OR' or N(R)(R');
- c) each occurrence of R⁴ is independently hydrogen, C₁₋₆aliphatic, CN, COR, COOR, CON(R)₂, or halogen;
- d) R⁵ is hydrogen, (CH₂)₃OR', (CH₂)₂OR', (CH₂)OR', (CH₂)₃N(R')₂, (CH₂)₂N(R')₂, (CH₂)N(R')₂, or C₁₋₄aliphatic;

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e) Q^3 is a direct bond, or is $-(CHR^6)_q-$, $-(CHR^6)_qO-$, $-(CHR^6)_qS-$, $-(CHR^6)_qS(O)_2-$, $-(CHR^6)_qS(O)-$, $-(CHR^6)_qNR-$, or $-(CHR^6)_qC(O)-$, wherein q is 0, 1, 2, or 3; and

f) Ar^2 is ring a, b, e, g, h, i, j, k, n, r, cc, dd, ff, jj, ll, or pp, wherein t is 0, 1, 2, or 3, and T is a bond or is an optionally substituted C_{1-6} alkylidene chain wherein one or two methylene units are optionally and independently replaced by $-O-$, $-NR-$, $-S-$, $-SO_2-$, $-COO-$, $-CO-$, $-OSO_2-$, $-NR(SO_2)-$, $-CONR-$, or $-SO_2NR-$, and R^7 is R' or halogen.

42. (Currently amended) The compound of claims 38, 39 or 40, wherein compound variables are selected from one of more of the following groups:

a) each occurrence of R^1 is independently hydrogen, halogen, $-CH_3$, $-CH_2CH_3$, $-OH$, $-OCH_3$, $-SCH_3$, $-NH_2$, $-N(CH_3)_2$, $-N(CH_2CH_3)_2$, $NH(CH_2)_2NHCH_3$, $NH(cyclopropyl)$, $NH(CH_2)cyclopropyl$, or $NH(CH_2)_2N(CH_3)_2$;

b) each occurrence of R^2 is independently hydrogen, halogen, Me, OH, OMe, NH_2 , or $N(Me)_2$;

c) each occurrence of R^4 is independently hydrogen, C_{1-6} aliphatic, CN, COR, COOR, $CON(R)_2$, or halogen;

d) R^5 is hydrogen, $(CH_2)_3OR'$, $(CH_2)_2OR'$, $(CH_2)OR'$, $(CH_2)_3N(R')_2$, $(CH_2)_2N(R')_2$, $(CH_2)N(R')_2$, or C_{1-4} aliphatic;

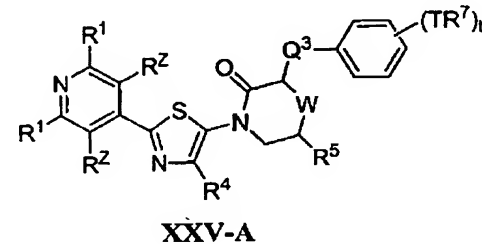
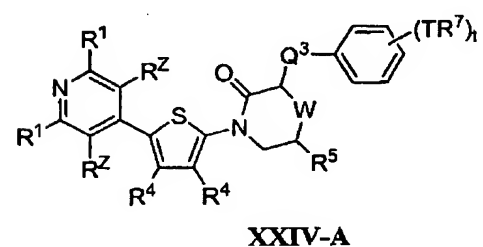
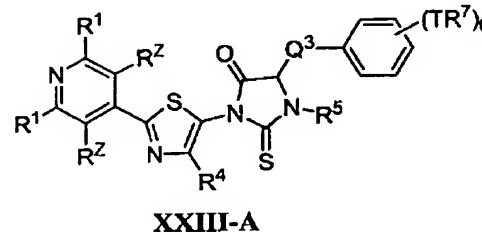
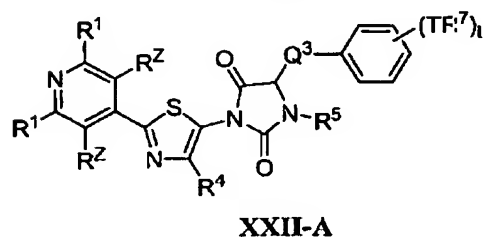
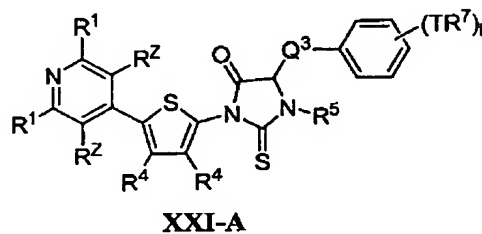
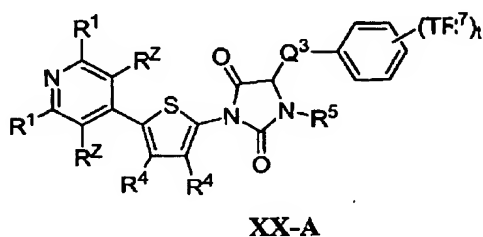
e) Q^3 is a direct bond, or is $-(CHR^6)_q-$, $-(CHR^6)_qO-$, $-(CHR^6)_qS-$, $-(CHR^6)_qS(O)_2-$, $-(CHR^6)_qS(O)-$, $-(CHR^6)_qNR-$, or $-(CHR^6)_qC(O)-$, wherein q is 0, 1, 2, or 3; and

f) Ar^2 is ring a, b, e, g, h, i, j, k, n, r, cc, dd, ff, jj, ll, or pp, wherein t is 0, 1, 2, or 3, and each occurrence of TR^7 is independently $-C_{1-3}$ alkyl, $-OR'$, $-SR'$, $-CF_3$, $-OCF_3$, $-SCF_3$, $-F$, $-Cl$, I , $-Br$, $-COOR'$, $-COR'$, $-O(CH_2)_4N(R)(R')$, $-O(CH_2)_3N(R)(R')$, $-O(CH_2)_2N(R)(R')$, $-O(CH_2)N(R)(R')$, $-O(CH_2)_4CON(R)(R')$,

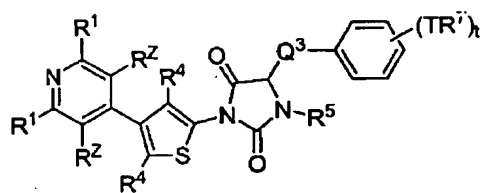
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-O(CH₂)₃CON(R)(R'), -O(CH₂)₂CON(R)(R'), -O(CH₂)CON(R)(R'), -C(O)N(R)(R'),
 -(CH₂)₄OR', -(CH₂)₃OR', -(CH₂)₂OR', -CH₂OR', optionally substituted phenyl or
 benzyl, -N(R)(R'), -(CH₂)₄N(R)(R'), -(CH₂)₃N(R)(R'), -(CH₂)₂N(R)(R'),
 -(CH₂)N(R)(R'), [[or]] -SO₂N(R)(R'), -NRSO₂R', -CON(R)(R'), or -OSO₂R'.

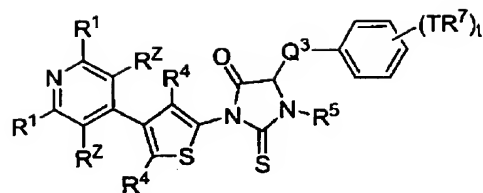
43. (Original) The compound of claims 38, 39 or 40, wherein Ar² is optionally substituted phenyl and compounds of general formula XX-A, through XXXVII are provided:



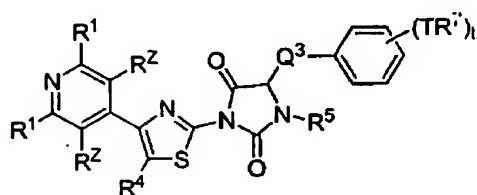
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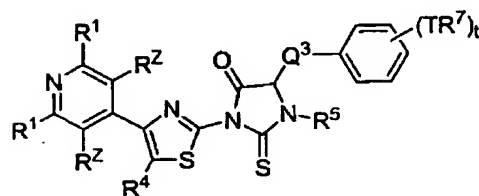
XXVI-A



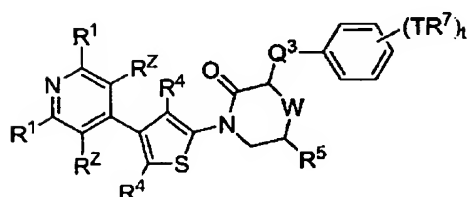
XXVII-A



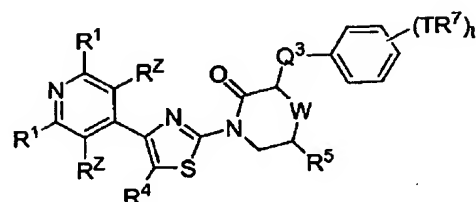
XXVIII-A



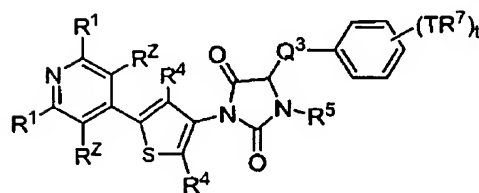
XXIX-A



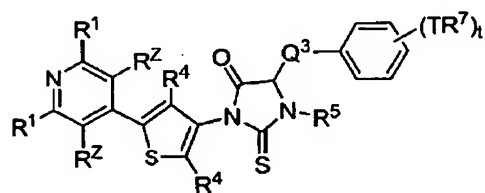
XXX-A



XXXI-A

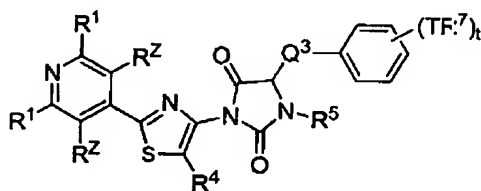


XXXII-A

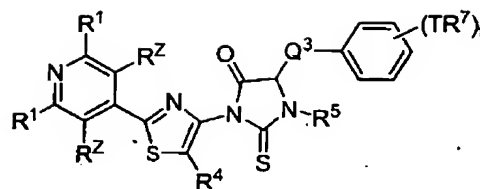


XXXIII-A

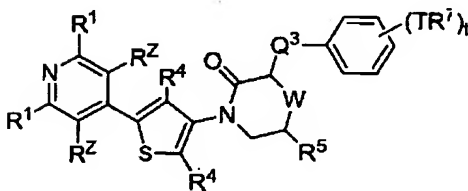
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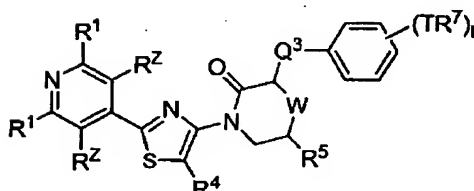
XXXIV-A



XXXV-A



XXXVI-A



XXXVII-A

44. (Currently amended) The compound of claim 43, wherein compound variables are selected from:

each occurrence of R^1 is hydrogen;

each occurrence of R^2 is hydrogen;

each occurrence of R^4 is independently hydrogen, C_{1-6} aliphatic, CN, COR, COOR, CON(R)₂, or halogen;

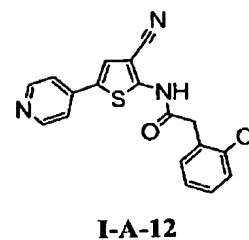
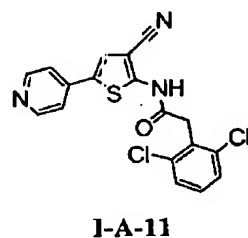
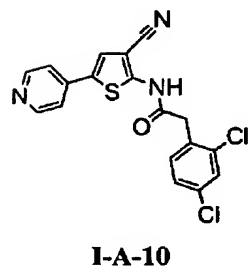
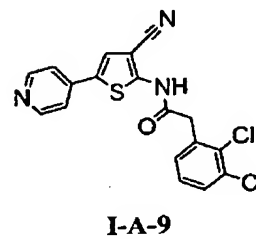
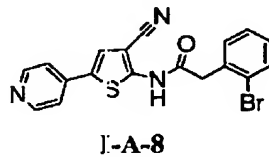
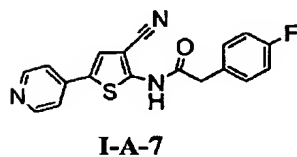
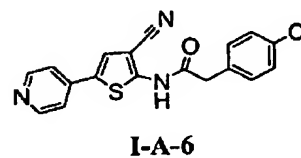
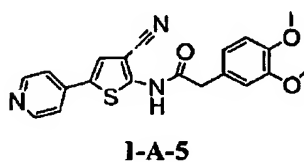
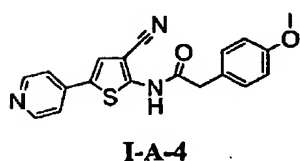
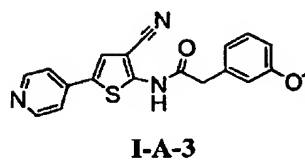
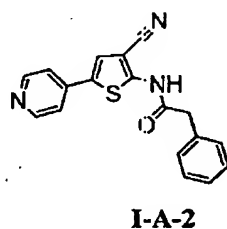
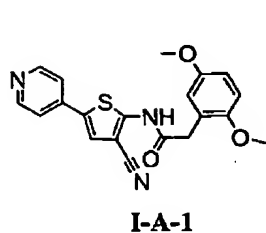
R^5 is hydrogen, $(CH_2)_3OR'$, $(CH_2)_2OR'$, $(CH_2)OR'$, $(CH_2)_3N(R')_2$, $(CH_2)_2N(R')_2$, $(CH_2)N(R')_2$, or C_{1-4} aliphatic;

Q^3 is a direct bond, or is $-(CHR^6)_q-$, $-(CHR^6)_qO-$, $-(CHR^6)_qS-$, $-(CHR^6)_qS(O)_2-$, $-(CHR^6)_qS(O)-$, $-(CHR^6)_qNR-$, or $-(CHR^6)_qC(O)-$, wherein q is 0, 1, 2, or 3; and

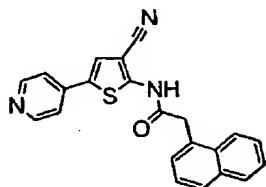
t is 0, 1, 2, or 3, and each occurrence of TR^7 is independently $-C_{1-3}$ alkyl, $-OR'$, $-SR'$, $-CF_3$, $-OCF_3$, $-SCF_3$, $-F$, $-Cl$, I , $-Br$, $-COOR'$, $-COR'$, $-O(CH_2)_4N(R)(R')$, $-O(CH_2)_3N(R)(R')$, $-O(CH_2)_2N(R)(R')$, $-O(CH_2)N(R)(R')$, $-O(CH_2)_4CON(R)(R')$, $-O(CH_2)_3CON(R)(R')$, $-O(CH_2)_2CON(R)(R')$, $-O(CH_2)CON(R)(R')$, $-C(O)N(R)(R')$, $-(CH_2)_4OR'$, $-(CH_2)_3OR'$, $-(CH_2)_2OR'$, $-CH_2OR'$, optionally substituted phenyl or benzyl, $-N(R)(R')$, $-(CH_2)_4N(R)(R')$, $-(CH_2)_3N(R)(R')$, $-(CH_2)_2N(R)(R')$, $-(CH_2)N(R)(R')$, $[[or]] -SO_2N(R)(R')$, $-NRSO_2R'$, $-CON(R)(R')$, or $-OSO_2R'$.

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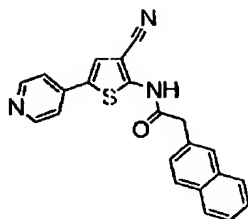
45. (Currently amended) The compound of claim 1, having one of the structures:



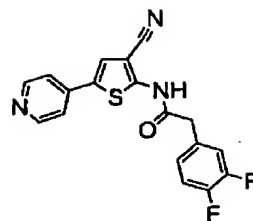
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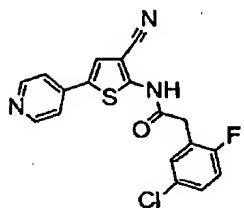
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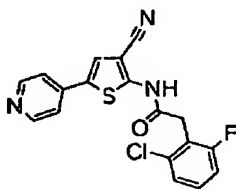
I-A-14



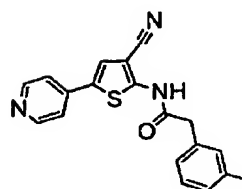
I-A-15



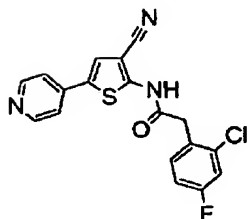
I-A-16



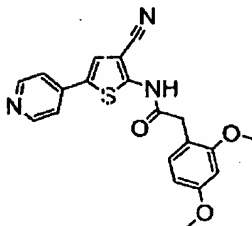
I-A-17



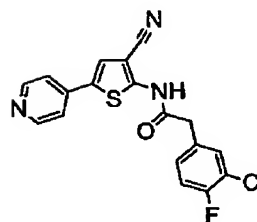
I-A-18



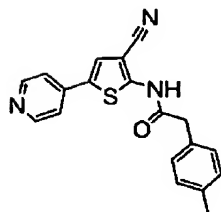
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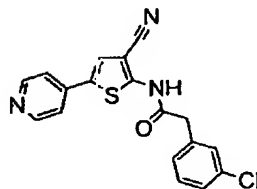
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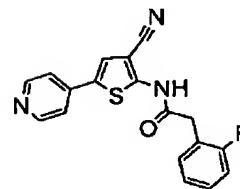
I-A-21



I-A-22

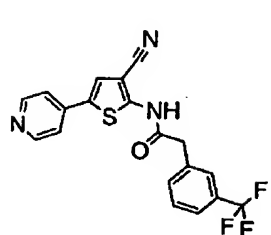
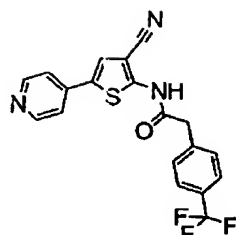
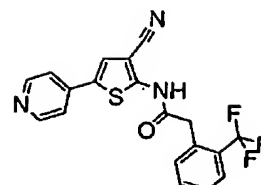
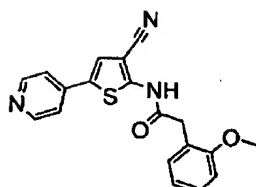
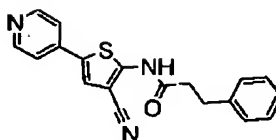
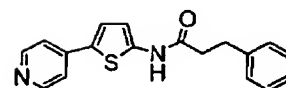
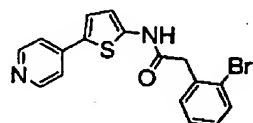
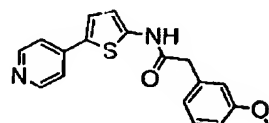
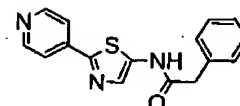
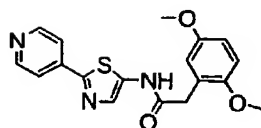
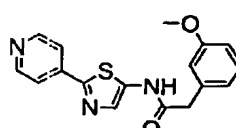
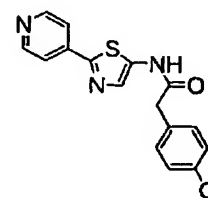


I-A-23

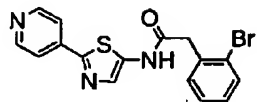


I-A-24

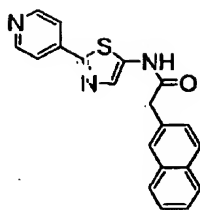
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**I-A-25****I-A-26****I-A-27****I-A-28****I-A-29****I-A-30****I-A-31****I-A-32****I-A-33****I-A-34****I-A-35****I-A-36**

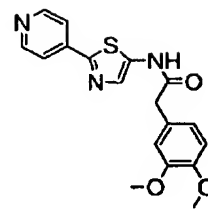
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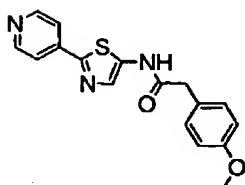
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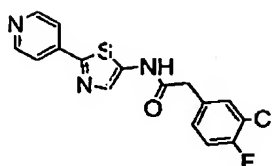
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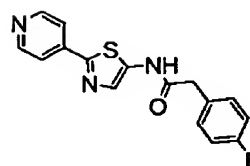
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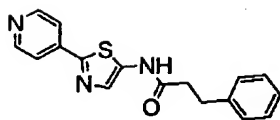
I-A-40



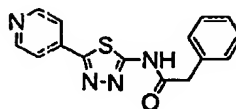
I-A-41



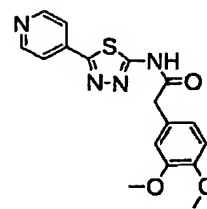
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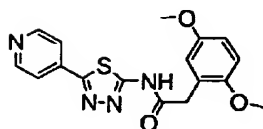
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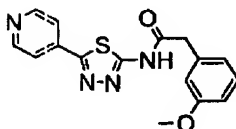
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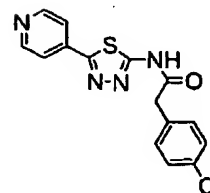
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I-A-46

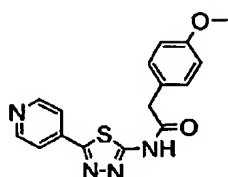


I-A-47

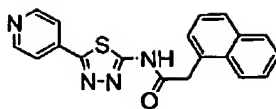


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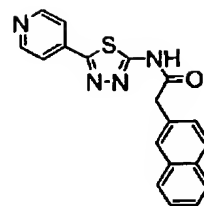
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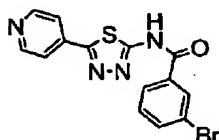
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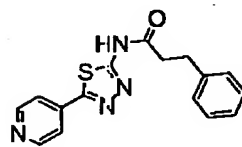
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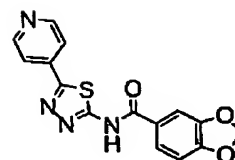
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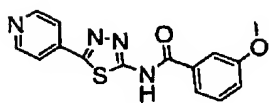
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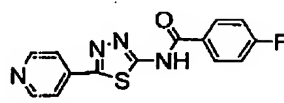
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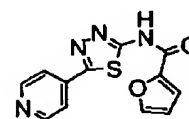
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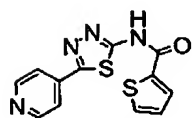
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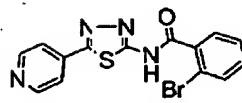
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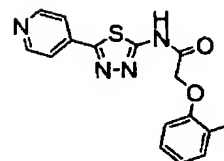
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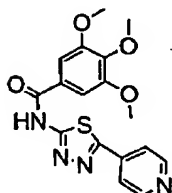
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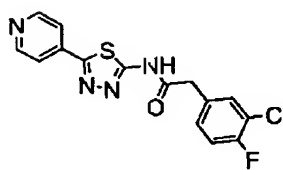
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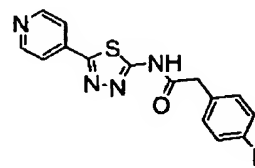
I-A-60



I-A-61

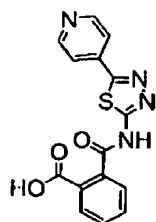
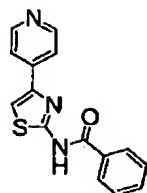
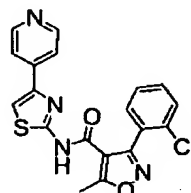
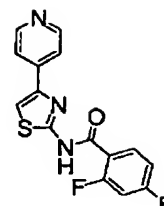
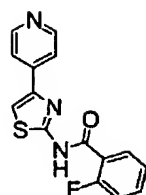
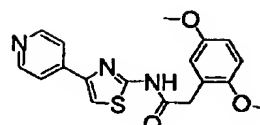
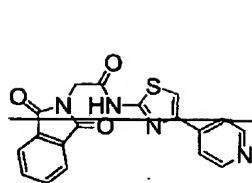
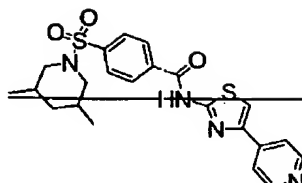
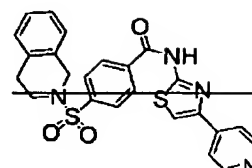
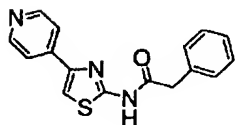
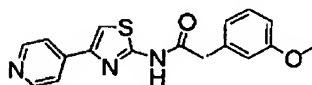
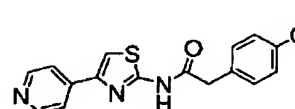


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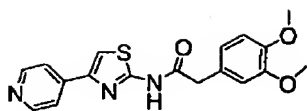
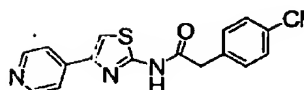
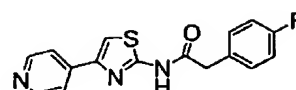
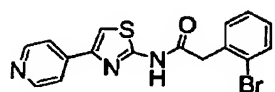
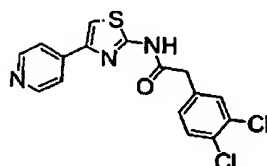
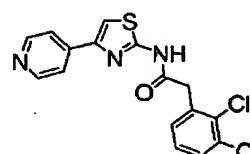
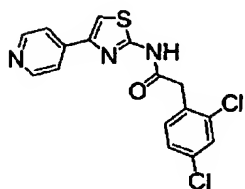
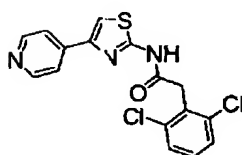
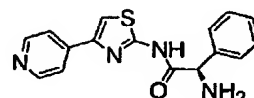
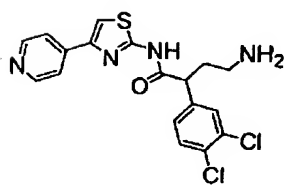
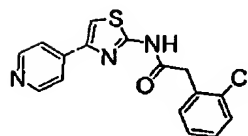
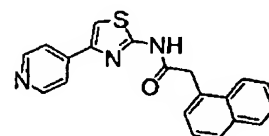
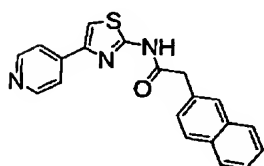
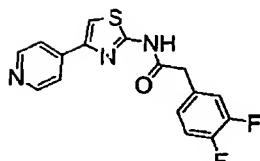
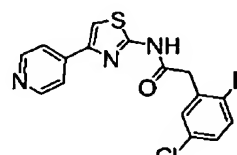


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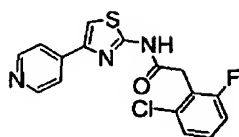
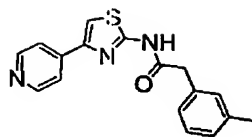
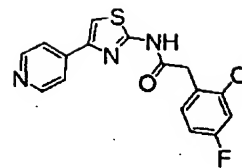
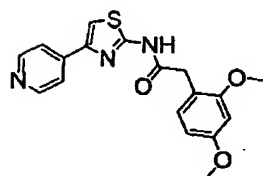
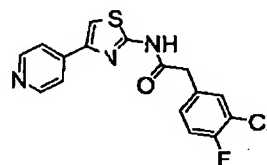
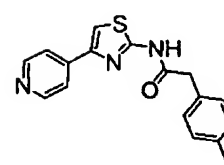
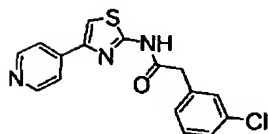
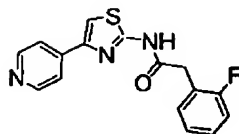
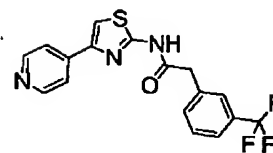
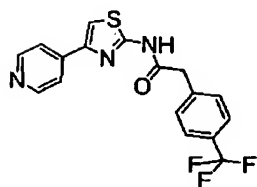
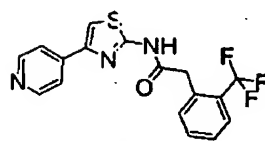
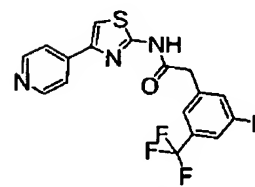
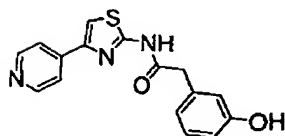
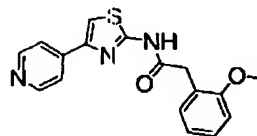
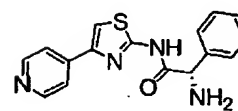
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**I-A-64****I-B-1****I-B-2****I-B-3****I-B-4****I-B-5****I-B-6****I-B-11****I-B-12****I-B-13****I-B-19****I-B-20****I-B-21**

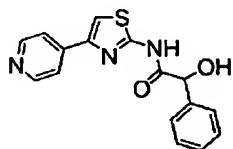
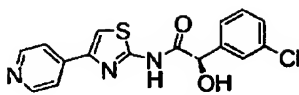
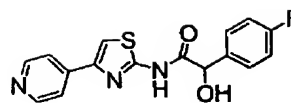
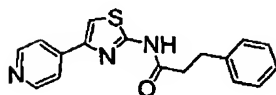
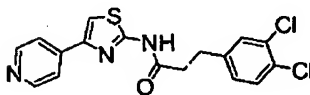
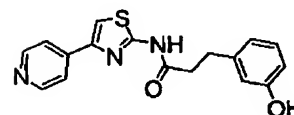
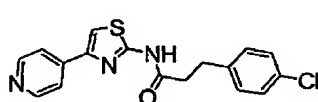
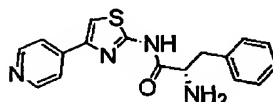
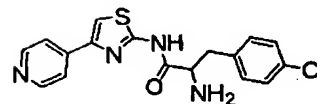
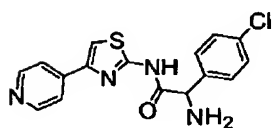
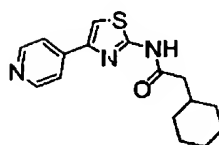
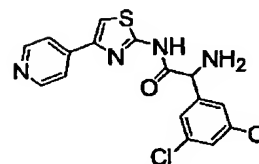
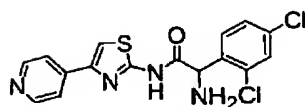
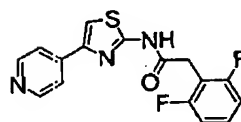
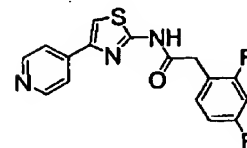
Attorney Docket No. VPI/02-115 US

**I-B-22****I-B-23****I-B-24****I-B-25****I-B-26****I-B-27****I-B-28****I-B-29****I-B-30****I-B-31****I-B-32****I-B-33****I-B-34****I-B-35****I-B-36**

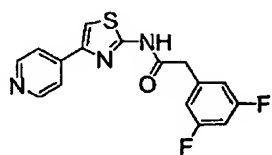
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**I-B-37****I-B-38****I-B-39****I-B-40****I-B-41****I-B-42****I-B-43****I-B-44****I-B-45****I-B-46****I-B-47****I-B-48****I-B-49****I-B-50****I-B-51**

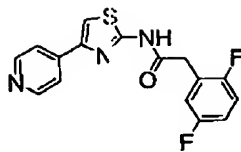
Applicants: Jingrong Cao et al.
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**I-B-52****I-B-53****I-B-54****I-B-55****I-B-56****I-B-57****I-B-58****I-B-59****I-B-60****I-B-61****I-B-62****I-B-63****I-B-64****I-B-65****I-B-66**

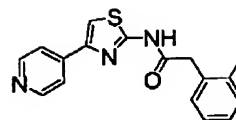
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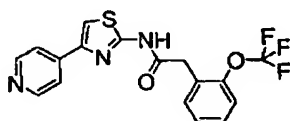
I-B-67



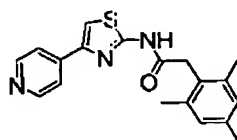
I-B-68



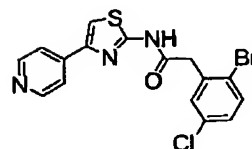
I-B-69



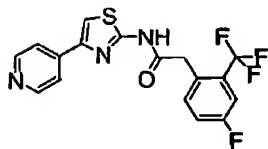
I-B-70



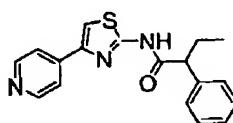
I-B-71



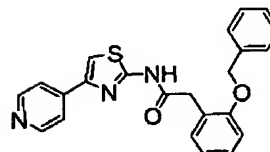
I-B-72



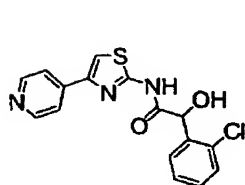
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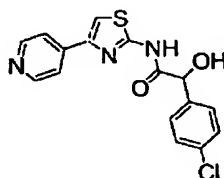
I-B-74



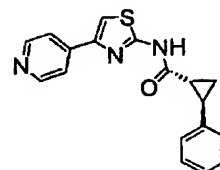
I-B-75



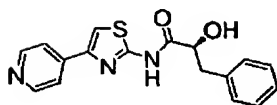
I-B-76



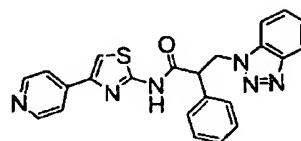
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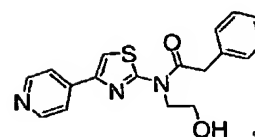
I-B-78



I-B-79

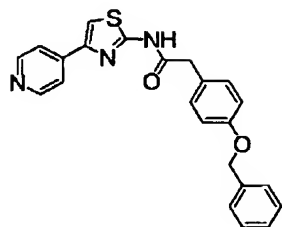
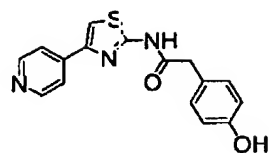
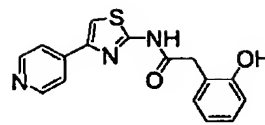
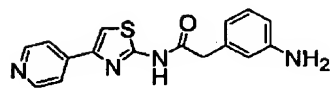
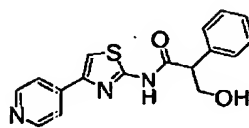
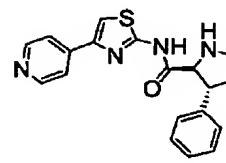
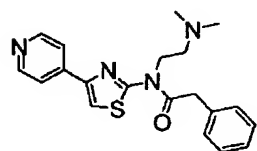
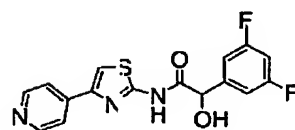
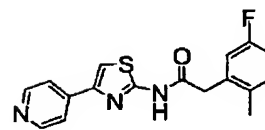
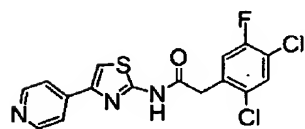
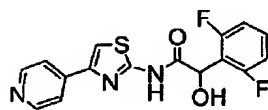
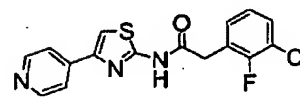
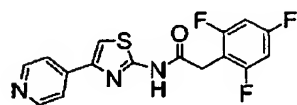
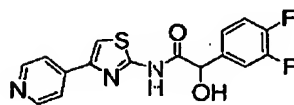
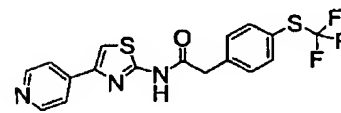


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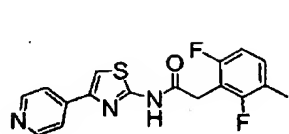
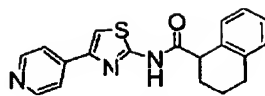
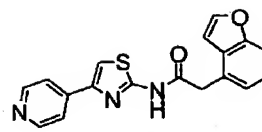
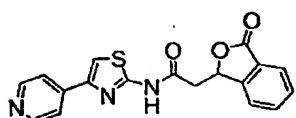
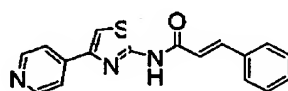
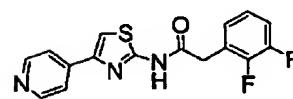
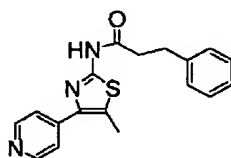
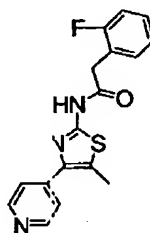
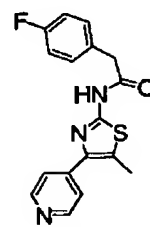
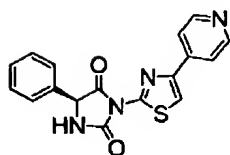
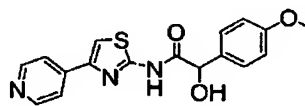
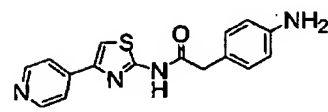
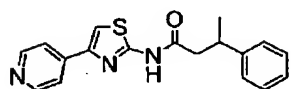
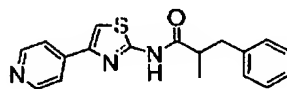
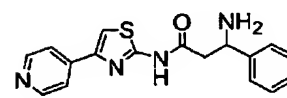


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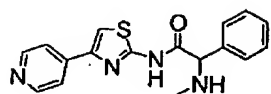
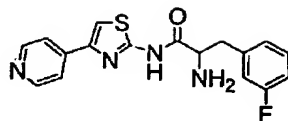
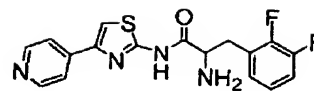
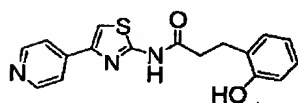
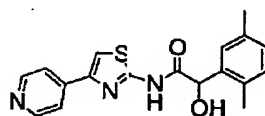
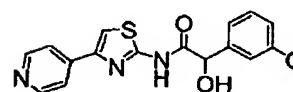
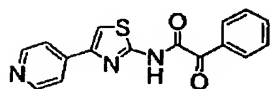
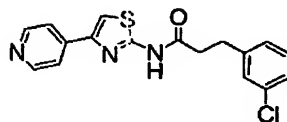
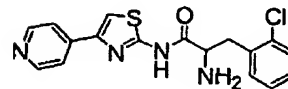
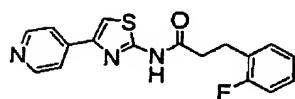
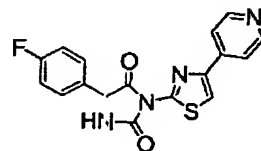
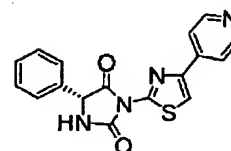
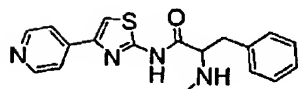
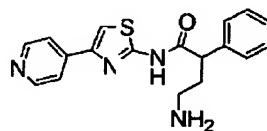
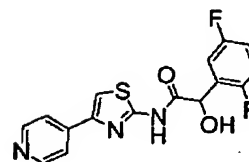
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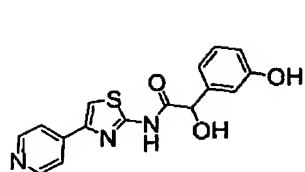
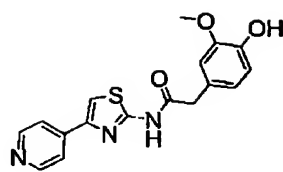
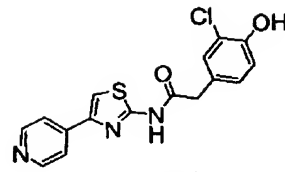
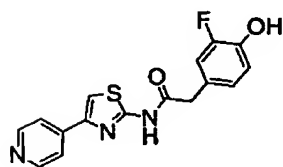
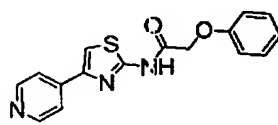
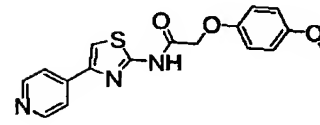
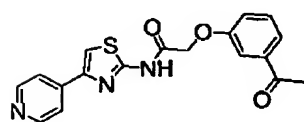
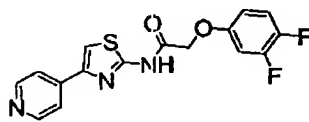
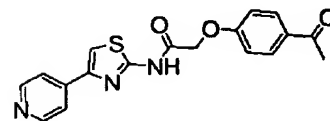
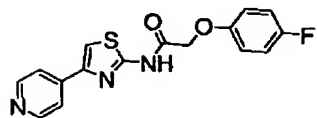
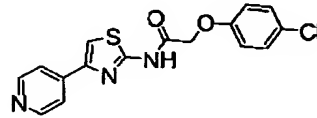
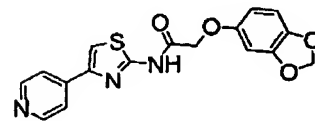
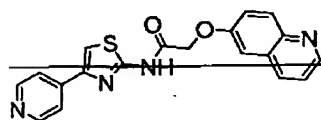
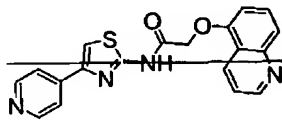
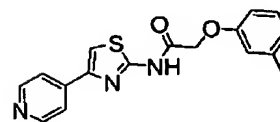
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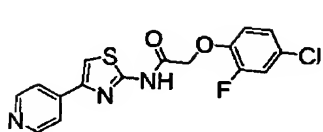
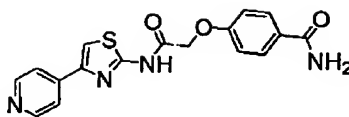
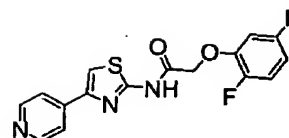
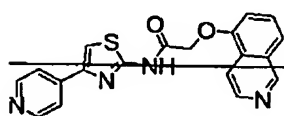
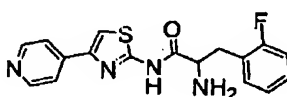
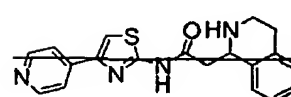
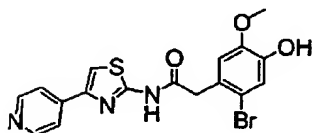
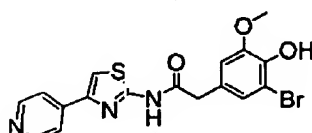
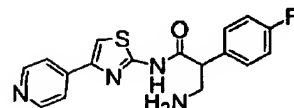
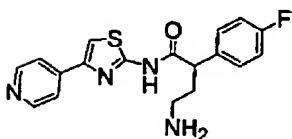
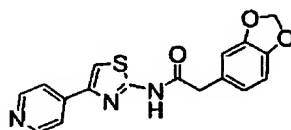
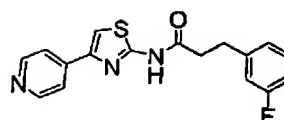
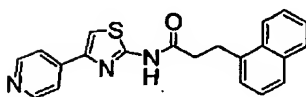
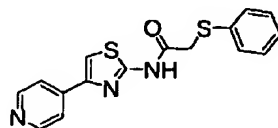
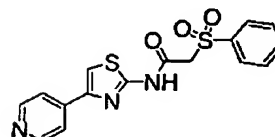
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**I-B-112****I-B-113****I-B-114****I-B-115****I-B-116****I-B-117****I-B-118****I-B-119****I-B-120****I-B-121****I-B-122****I-B-123****I-B-124****I-B-125****I-B-126**

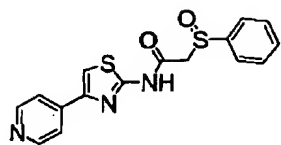
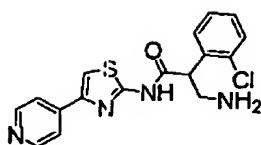
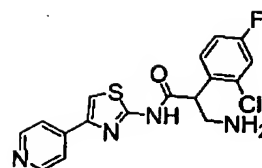
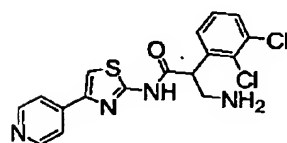
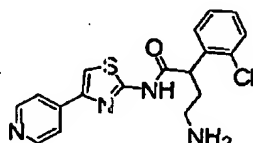
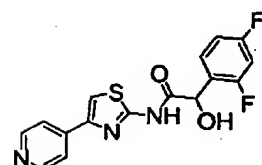
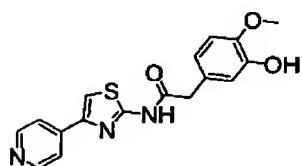
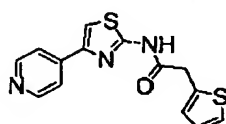
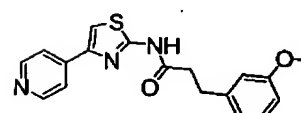
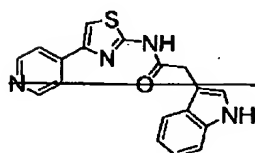
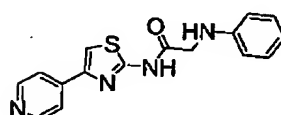
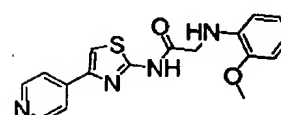
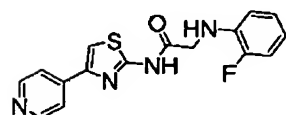
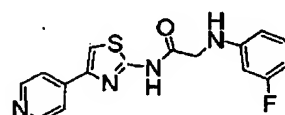
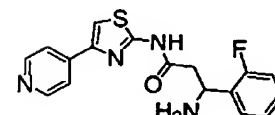
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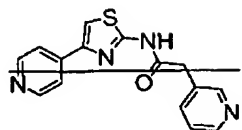
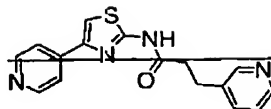
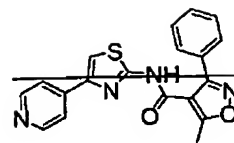
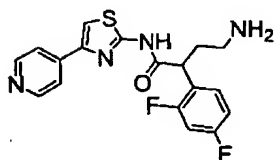
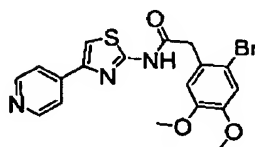
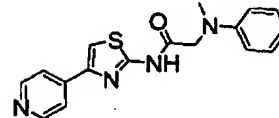
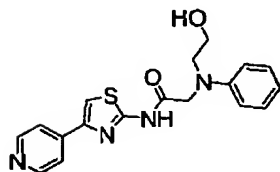
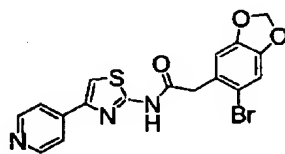
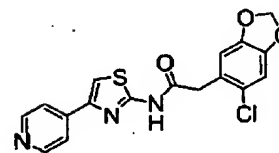
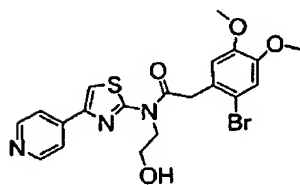
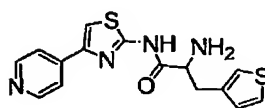
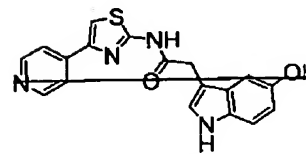
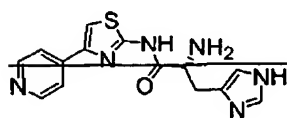
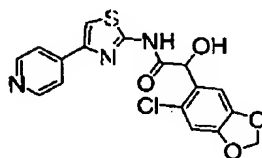
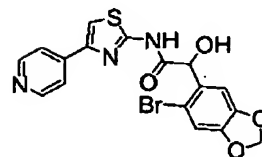
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**I-B-142****I-B-143****I-B-144****I-B-145****I-B-146****I-B-147****I-B-148****I-B-149****I-B-150****I-B-151****I-B-152****I-B-153****I-B-154****I-B-155****I-B-156**

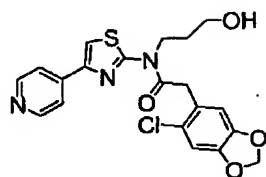
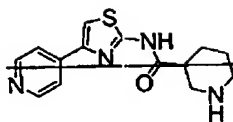
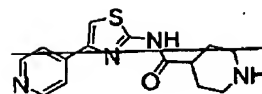
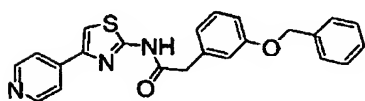
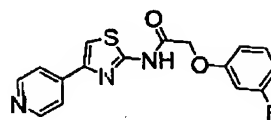
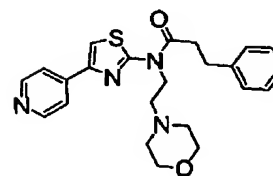
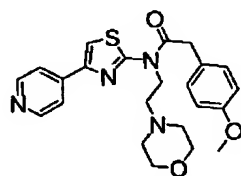
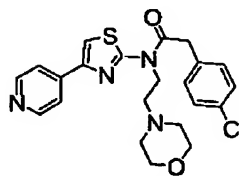
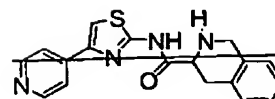
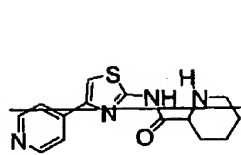
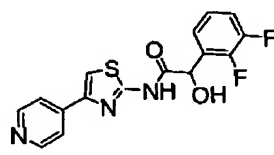
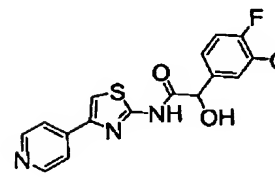
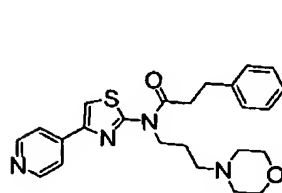
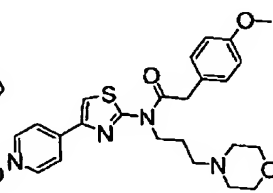
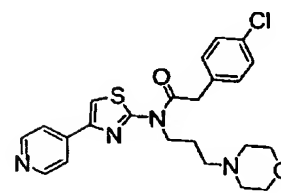
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**I-B-157****I-B-158****I-B-159****I-B-160****I-B-161****I-B-162****I-B-163****I-B-164****I-B-165****I-B-166****I-B-167****I-B-168****I-B-169****I-B-170****I-B-171**

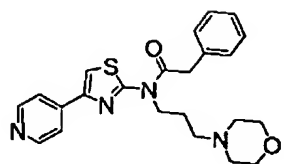
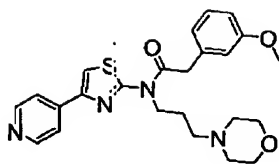
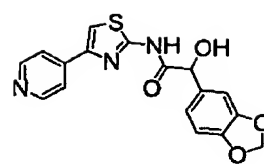
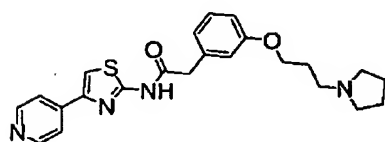
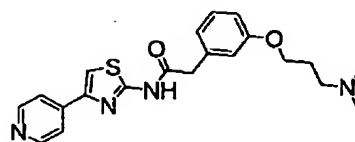
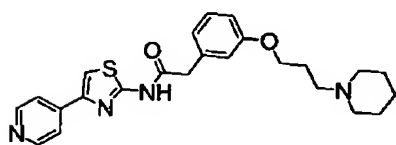
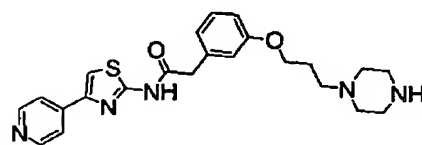
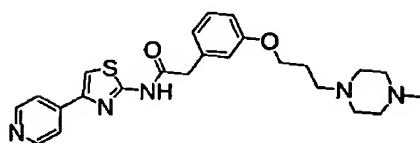
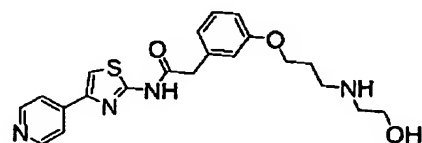
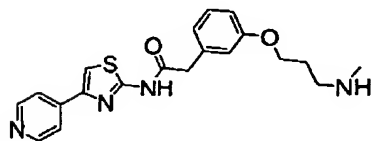
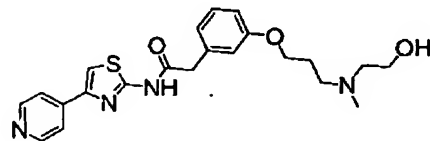
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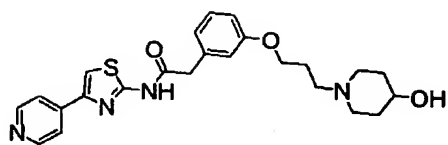
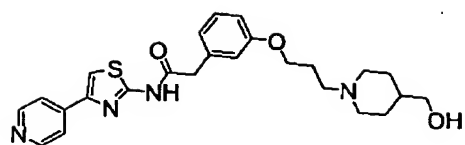
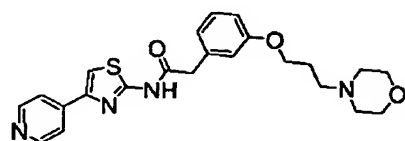
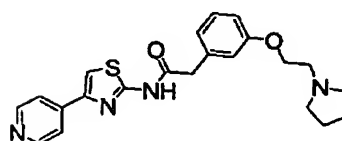
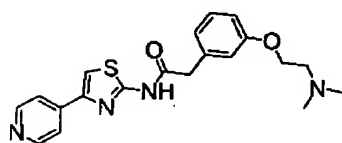
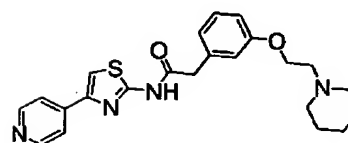
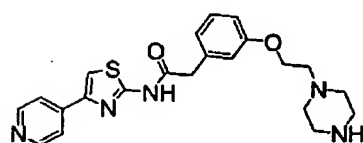
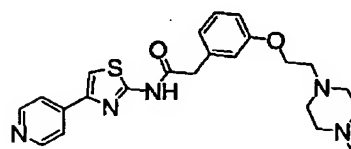
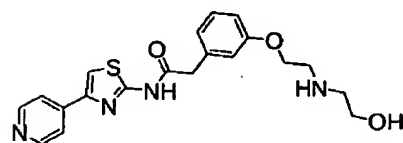
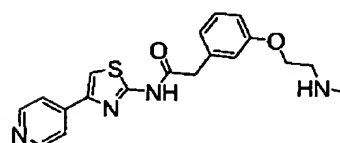
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**I-B-187****I-E-188****I-B-189****I-B-190****I-B-191****I-B-192****I-B-193****I-B-194****I-B-195****I-B-196****I-B-197****I-B-198****I-B-199****I-B-200****I-B-201**

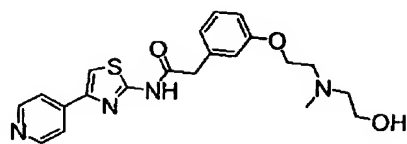
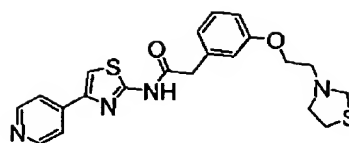
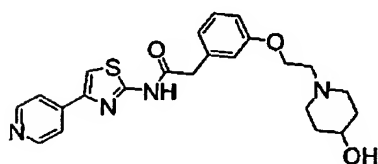
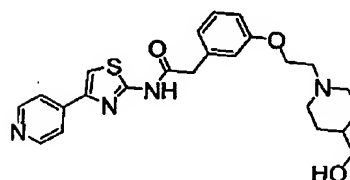
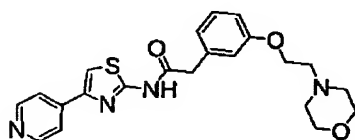
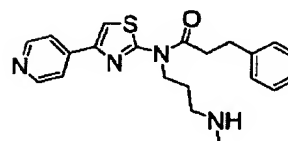
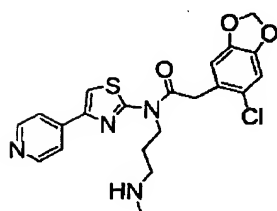
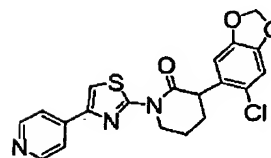
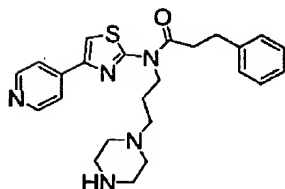
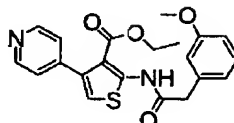
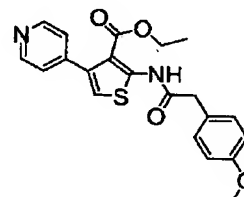
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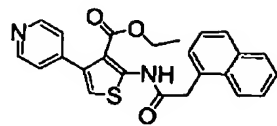
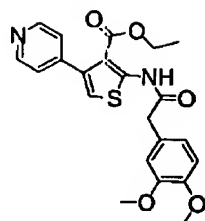
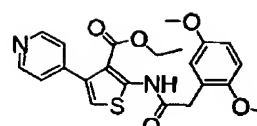
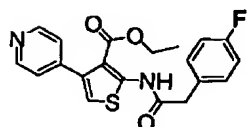
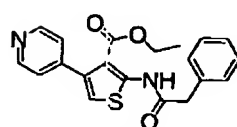
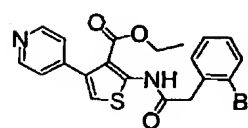
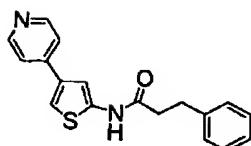
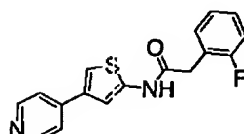
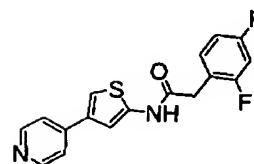
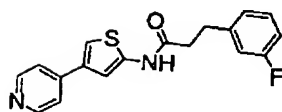
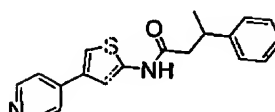
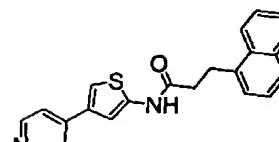
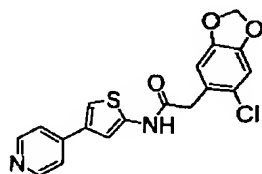
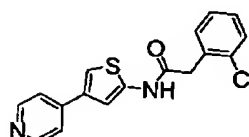
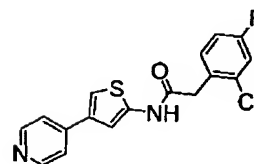
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**I-B-213****I-B-214****I-B-215****I-B-216****I-B-217****I-B-218****I-B-219****I-B-220****I-B-221****I-B-222**

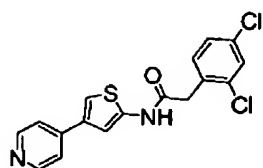
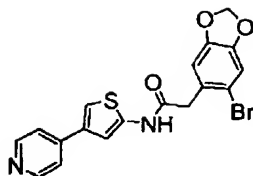
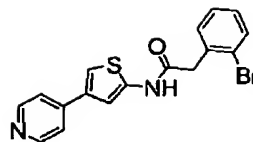
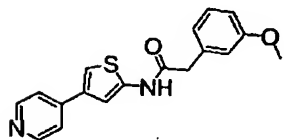
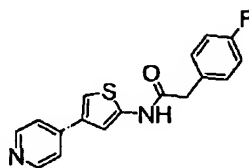
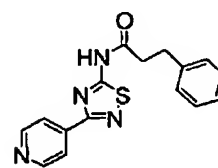
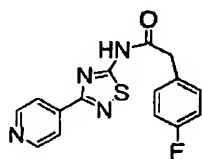
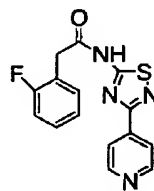
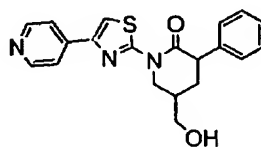
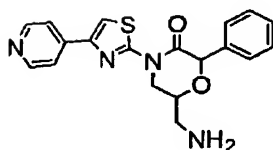
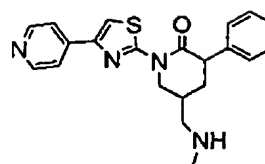
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**I-B-223****I-B-224****I-B-225****I-B-226****I-B-227****I-B-228****I-B-229****I-B-230****I-B-231****I-B-232****I-B-233**

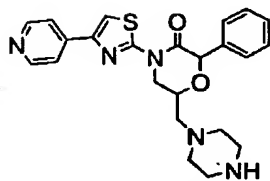
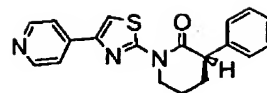
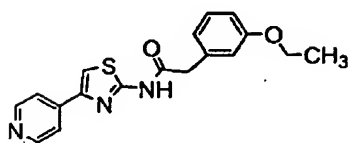
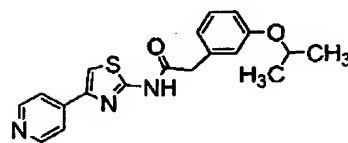
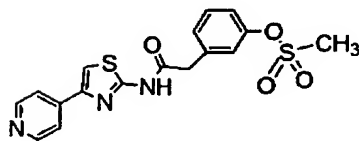
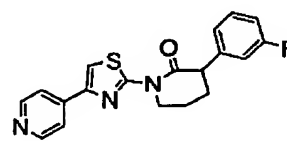
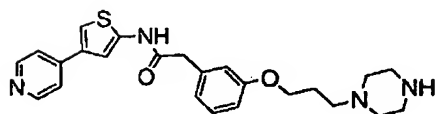
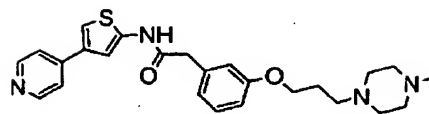
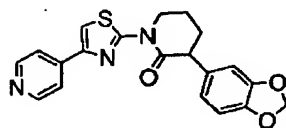
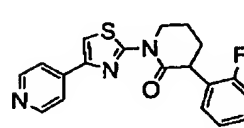
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**I-B-234****I-B-235****I-B-236****I-B-237****I-B-238****I-B-239****I-B-240****I-B-241****I-B-242****I-B-243****I-B-244****I-B-245****I-B-246****I-B-247****I-B-248**

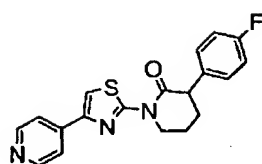
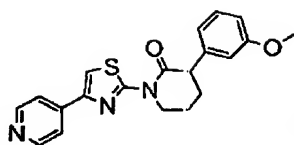
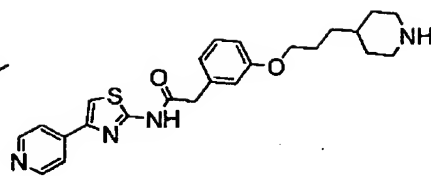
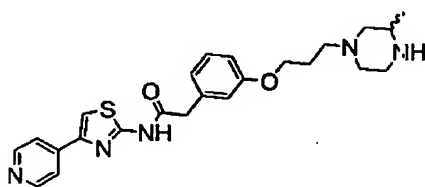
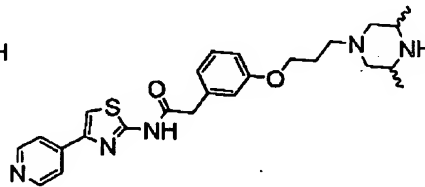
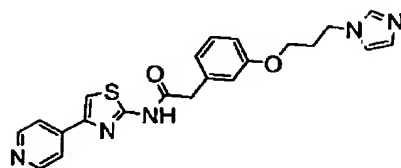
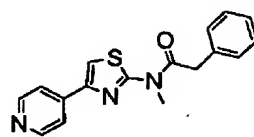
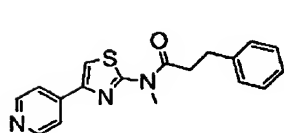
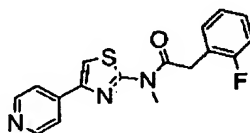
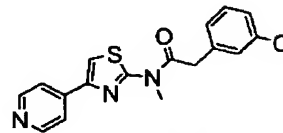
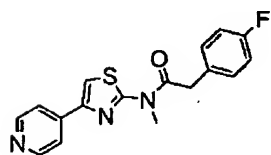
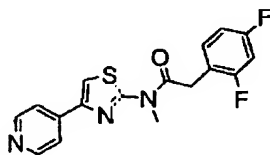
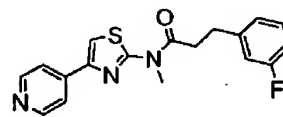
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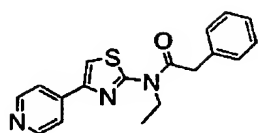
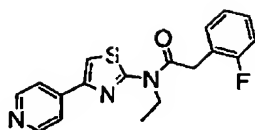
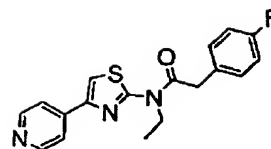
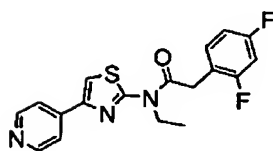
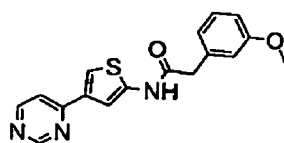
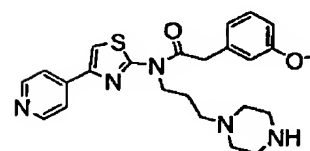
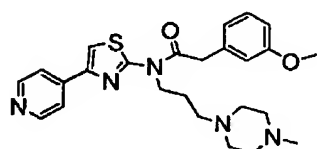
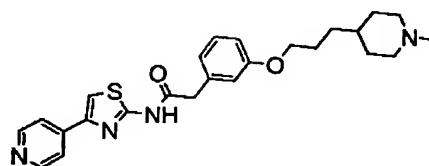
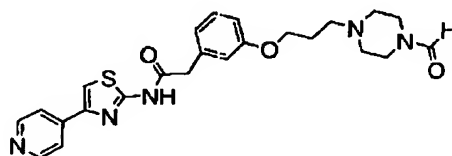
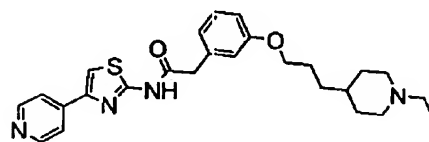
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**I-B-278****I-B-279****I-B-280****I-B-281****I-B-282****I-B-283****I-B-284****I-B-285****I-B-286****I-B-287**

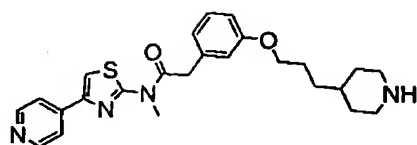
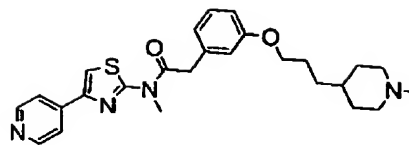
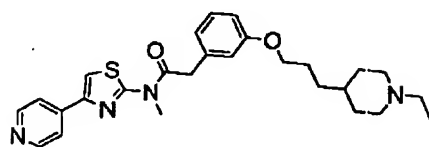
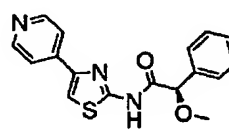
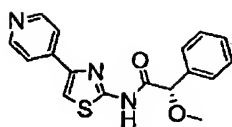
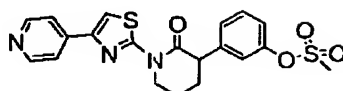
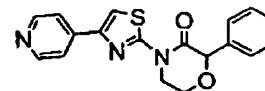
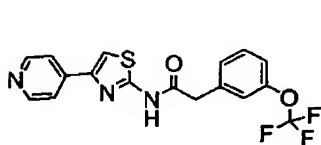
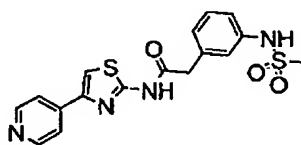
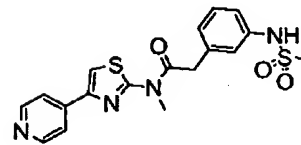
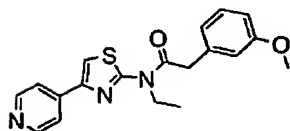
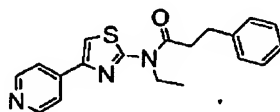
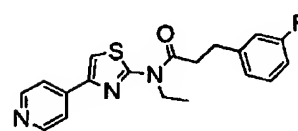
Applicants: Jingrong Cao et al.
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**I-B-288****I-B-289****I-B-290****I-B-291****I-B-292****I-B-293****I-B-294****I-B-295****I-B-296****I-B-297****I-B-298****I-B-299****I-B-300**

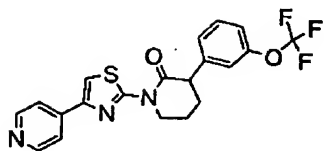
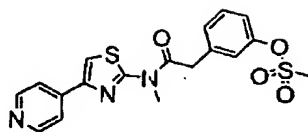
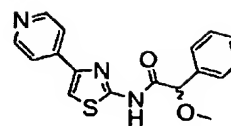
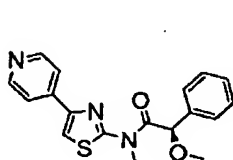
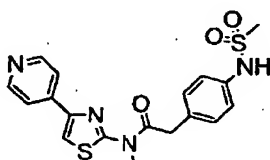
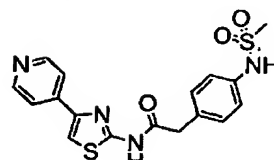
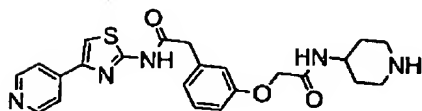
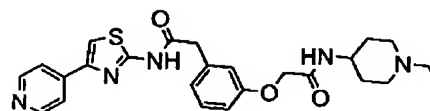
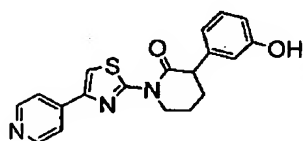
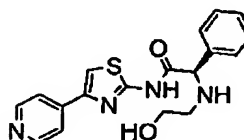
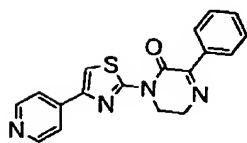
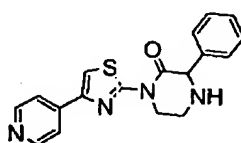
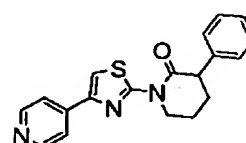
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**I-B-301****I-B-302****I-B-303****I-B-304****I-B-305****I-B-306****I-B-307****I-B-308****I-B-309****I-B-312**

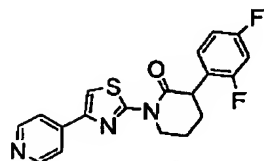
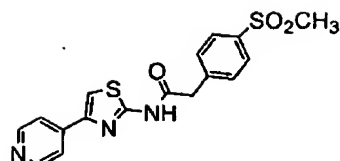
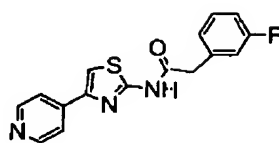
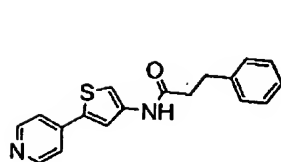
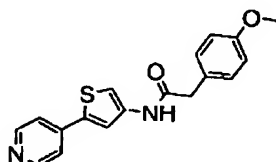
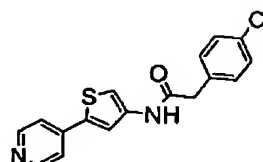
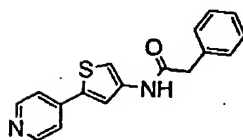
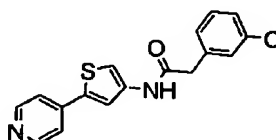
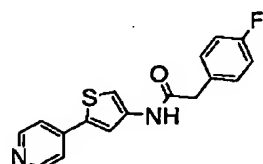
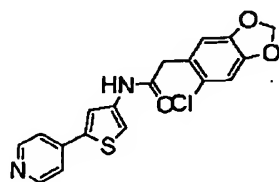
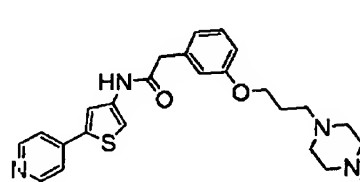
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**I-B-313****I-B-314****I-B-315****I-B-321****I-B-322****I-B-323****I-B-324****I-B-325****I-B-326****I-B-327****I-B-328****I-B-329****I-B-330**

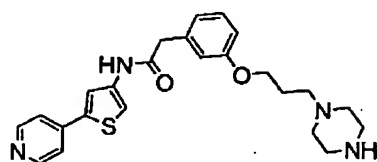
Applicants: Jingrong Cao et al.
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**I-B-331****I-B-332****I-B-333****I-B-334****I-B-335****I-B-336****I-B-337****I-B-338****I-B-339****I-B-340****I-B-341****I-B-342****I-B-343**

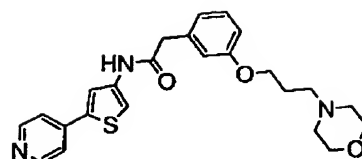
Applicants: Jingrong Cao et al.
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**I-B-344****I-B-345****I-E-346****I-C-1****I-C-2****I-C-3****I-C-4****I-C-5****I-C-6****I-C-7****I-C-8**

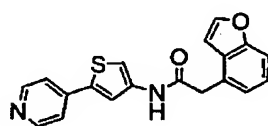
Applicants: Jingrong Cao et al.
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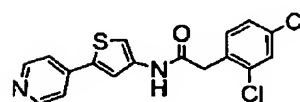
I-C-9



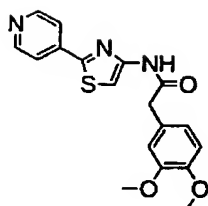
I-C-10



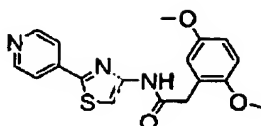
I-C-11



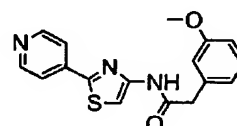
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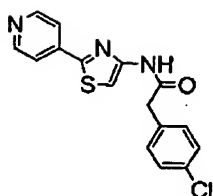
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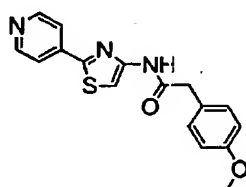
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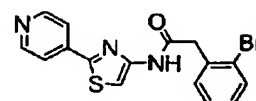
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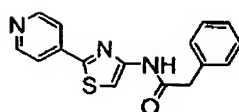
I-C-16



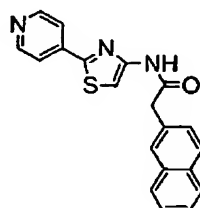
I-C-17



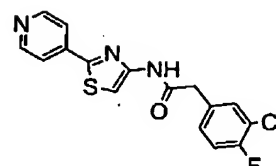
I-C-18



I-C-19

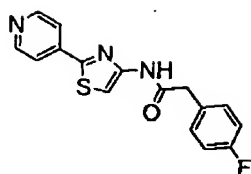


I-C-20

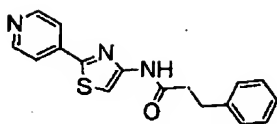


I-C-21

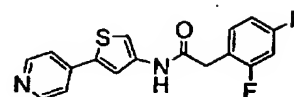
Attorney Docket No. VPI/02-115 US



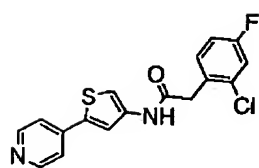
I-C-22



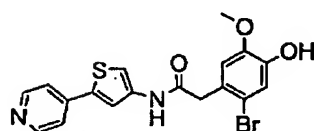
I-C-23



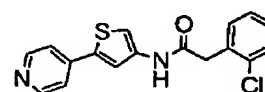
I-C-24



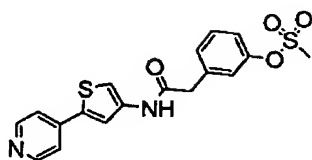
I-C-25



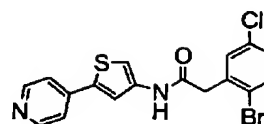
I-C-26



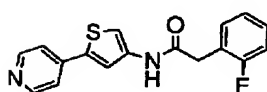
I-C-27



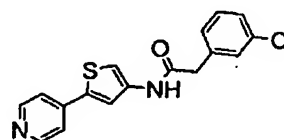
I-C-28



I-C-30

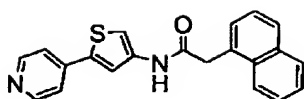


I-C-31

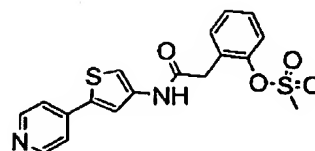


I-C-32

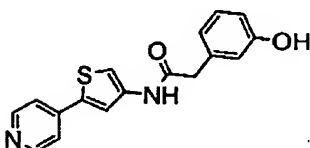
Attorney Docket No. VPI/02-115 US



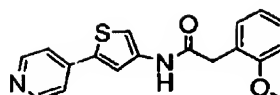
I-C-34



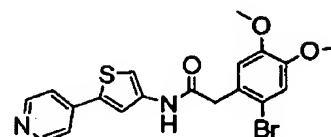
I-C-36



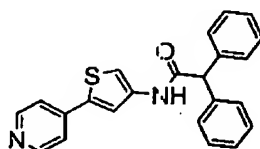
I-C-37



I-C-38



I-C-39



I-C-41

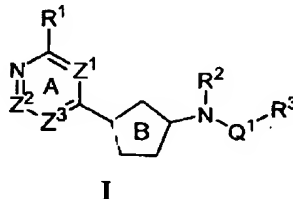
46. (Original) A composition comprising an effective amount of compound of claim 1, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

47. (Currently amended) The composition of claim 46, additionally comprising a therapeutic agent selected from a chemotherapeutic or anti-proliferative agent selected from mechlorethamine, chlorambucil, cyclophosphamide, melphalan, ifosfamide, methotrexate, 6-mercaptopurine, 5-fluorouracil, cytarabine, gemcitabine, vinblastine, vincristine, vinorelbine, paclitaxel, etoposide, irinotecan, topotecan, doxorubicin, bleomycin, mitomycin, carmustine, lomustine, cisplatin, carboplatin, asparaginase, tamoxifen, leuprolide, flutamide, and megestrol, imatinib mesylate, adriamycin, dexamethasone, or cyclophosphamide; [[,]] an anti-inflammatory agent selected from

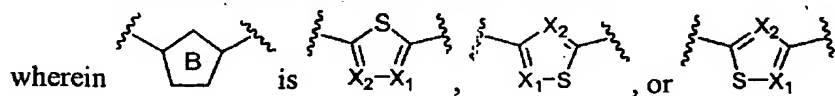
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~~albuterol or Singulair; an immunomodulatory or immunosuppressive agent, a neurotrophic factor, or an agent for treating cardiovascular disease selected from a beta-blocker, an ACE inhibitors, s diuretic, a nitrate, a calcium channel blocker, or a statin, an agent for treating destructive bone disorders, an agent for treating liver disease, an anti-viral agent, an agent for treating blood disorders, an agent for treating diabetes, or an agent for treating immunodeficiency disorders.~~

48. (Currently amended) A method of inhibiting ROCK, ERK, GSK, or AGC kinase activity in vitro in a biological sample selected from a cell culture or extract thereof biopsied material obtained from a mammal or an extract thereof, saliva, urine, feces, semen, or tears; said method comprising contacting said biological sample with a compound having the formula:



or a pharmaceutically acceptable salt thereof, wherein:



R^1 is halogen, CN, NO_2 , or V_mR ;

Z^1 and Z^3 are each independently CR^Z ; and Z^2 is CR^1 ;

each occurrence of R^Z is independently halogen, CN, NO_2 , or $\text{U}_n\text{R}'$;

R^2 is $\text{U}_n\text{R}'$;

X^1 and X^2 are each independently CR^4 or N;

each occurrence of R^4 is independently halogen, CN, NO_2 , or V_mR ;

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each occurrence of U or V is independently an optionally substituted C_{1-6} alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by $-NR-$, $-S-$, $-O-$, $-CS-$, $-CO_2-$, $-OCO-$, $-CO-$, $-COCO-$, $-CONR-$, $-NRCO-$, $-NRCO_2-$, $-SO_2NR-$, $-NRSO_2-$, $-CONRNR-$, $-NRCONR-$, $-OCONR-$, $-NRNR-$, $-NRSO_2NR-$, $-SO-$, or $-SO_2-$, ~~$P(O)$, $P(O)_2$, or $P(OR')$~~ ;

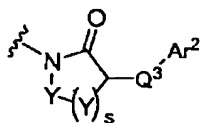
m and n are each independently 0 or 1;

each occurrence of R is independently hydrogen or an optionally substituted C_{1-6} aliphatic group; and each occurrence of R' is independently hydrogen or an optionally substituted C_{1-6} aliphatic group, a 3-8-membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or R and R' , two occurrences of R, or two occurrences of R' , are taken together with the atom(s) to which they are bound to form an optionally substituted 3-12 membered saturated, partially unsaturated, or fully unsaturated monocyclic or bicyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

Q^1 is $-CO-$, $-SO_2-$, or $-SO_2NR-$;

R^3 is Q^2-Ar^1 ,

or R^2 and Q^1-R^3 , taken together with the nitrogen atom, form the cyclic group:



, where s is 1 or 2, each occurrence of Y is independently, as valency and stability permit, $-CO-$, $-CS-$, $-SO_2-$, $-O-$, $-S-$, $-NR^5-$, or $-C(R^5)_2-$, and R^5 is U_nR' ;

Q^2 and Q^3 are each independently a bond or a C_{1-6} alkylidene chain, wherein up to two methylene units of the chain are each optionally and independently replaced by $-S-$, $-O-$, $-CS-$, $-CO_2-$, $-OCO-$, $-CO-$, $-COCO-$, $-CONR'-$, $-NR'CO-$, $-NR'CO_2-$, $-SO_2NR'-$,

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-NR'SO₂-, -CONR'NR'-, -NR'CONR'-, -OCONR'-, -NR'NR'-, -NR'SO₂NR'-, -SO-, or -SO₂-, ~~P(O)-, P(O)₂-, or P(OR')-~~; and wherein any carbon atom in the one or more methylene units is optionally substituted with one or two occurrences of R⁶, wherein each occurrence of R⁶ is independently halogen, CN, NO₂, or U_nR', or two occurrences of R⁶, or R' and R⁶, taken together with the atoms to which they are bound, form an optionally substituted 3-6-membered cycloalkyl, heterocyclyl, aryl or heteroaryl ring; and

~~Ar¹ and Ar² are each independently is~~ a 5-8 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from ~~nitrogen~~, oxygen[[,]] or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from ~~nitrogen~~, oxygen[[,]] or sulfur; wherein Ar¹ ~~is~~ and Ar² ~~are~~ each optionally substituted with 0-5 independent occurrences of TR⁷; wherein T is a bond or is a C₁-C₆ alkylidene chain wherein up to two methylene units of T are optionally and independently replaced by -NR-, -S-, -O-, -CS-, -CO₂-, -OCO-, -CO-, -COCO-, -CONR-, -NRCO-, -NRCO₂-, -SO₂NR-, -NRSO₂-, -CONRNR-, -NRCONR-, -OCONR-, -NRNR-, -NRSO₂NR-, -SO-, or -SO₂-, ~~P(O)-, P(O)₂-, or P(OR')-~~;

Ar² is a 5-8 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein Ar² is optionally substituted with 0-5 independent occurrences of TR⁷; wherein T is a bond or is a C₁-C₆ alkylidene chain wherein up to two methylene units of T are optionally and independently replaced by -NR-, -S-, -O-, -CS-, -CO₂-, -OCO-, -CO-, -COCO-, -CONR-, -NRCO-, -NRCO₂-, -SO₂NR-, -NRSO₂-, -CONRNR-, -NRCONR-, -OCONR-, -NRNR-, -NRSO₂NR-, -SO-, or -SO₂-; and

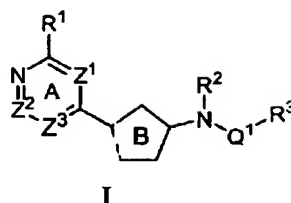
each occurrence of R⁷ is independently R', halogen, NO₂, or CN;
 or a pharmaceutically acceptable salt or composition thereof.

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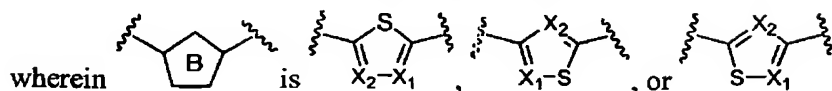
49. (Original) The method of claim 48, wherein the method comprises inhibiting ROCK activity.

50. (Currently amended) A method of treating or lessening the severity of a proliferative disorder selected from breast cancer, ovarian cancer, ~~cervical cancer,~~ prostate cancer, ~~testicular cancer, cancer of the genitourinary tract, esophageal cancer,~~ cancer of the larynx, glioblastoma, neuroblastoma, stomach cancer, skin cancer, keratoacanthoma, lung cancer, epidermoid carcinoma, large cell carcinoma, small cell carcinoma, lung adenocarcinoma, bone cancer, colon cancer, adenoma, cancer of of ~~of~~ ~~the~~ ~~pancreas, adenocarcinoma, thyroid cancer, follicular carcinoma, undifferentiated carcinoma, papillary carcinoma, seminoma, melanoma, sarcoma, bladder carcinoma, cancer of the liver and biliary passages, or kidney carcinoma, myeloid disorders, lymphoid disorders, Hodgkin's, hairy cell carcinoma, cancer of the buccal cavity and pharynx, cancer of the lip, tongue cancer, cancer of the pharynx, cancer of the small intestine, colorectal cancer, cancer of the large intestine, rectal cancer, brain cancer, or leukemia; cardiovascular disease selected from cardiomegaly, hypertension, angina pectoris, cerebrovascular contraction, cerebral vasospasm, coronary vasospasm, myocardial hypertrophy, ischemia/reperfusion induced injury, endothelial dysfunction, or erectile dysfunction; a neurodegenerative disorder selected from Alzheimer's disease, Huntington's disease, Parkinson's disease, basal ganglia movement disorders, chorea, dystonia, Wilson's Disease, Pick's Disease, frontal lobe degeneration, progressive supranuclear palsy (PSP), Creutzfeldt-Jakob Disease, tau pathology, or corticobasal degeneration; an inflammatory disorder selected from allergy or asthma; or diabetes, comprising the step of administering to said patient a compound having the formula:~~

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or a pharmaceutically acceptable salt thereof, wherein:



R^1 is halogen, CN, NO_2 , or V_mR ;

Z^1 and Z^3 are each independently CR^Z ; and Z^2 is CR^1 ;

each occurrence of R^Z is independently halogen, CN, NO_2 , or U_nR' ;

R^2 is U_nR' ;

X^1 and X^2 are each independently CR^4 or N;

each occurrence of R^4 is independently halogen, CN, NO_2 , or V_mR ;

each occurrence of U or V is independently an optionally substituted C_{1-6} alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by $-NR-$, $-S-$, $-O-$, $-CS-$, $-CO_2-$, $-OCO-$, $-CO-$, $-COCO-$, $-CONR-$, $-NRCO-$, $-NRCO_2-$, $-SO_2NR-$, $-NRSO_2-$, $-CONRNR-$, $-NRCONR-$, $-OCONR-$, $-NRNR-$, $-NRSO_2NR-$, $-SO-$, or $-SO_2-$, $\underline{P(O)}$, $\underline{P(O)}_2$, or $\underline{P(OR')}$;

m and n are each independently 0 or 1;

each occurrence of R is independently hydrogen or an optionally substituted C_{1-6} aliphatic group; and each occurrence of R' is independently hydrogen or an optionally substituted C_{1-6} aliphatic group, a 3-8-membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or R and R' , two occurrences of R, or two occurrences of R' ,

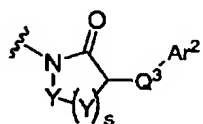
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are taken together with the atom(s) to which they are bound to form an optionally substituted 3-12 membered saturated, partially unsaturated, or fully unsaturated monocyclic or bicyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

Q^1 is $-CO-$, $-SO_2-$, or $-SO_2NR-$;

R^3 is Q^2-Ar^1 ,

or R^2 and Q^1-R^3 , taken together with the nitrogen atom, form the cyclic group:



, where s is 1 or 2, each occurrence of Y is independently, as valency and stability permit, $-CO-$, $-CS-$, $-SO_2-$, $-O-$, $-S-$, $-NR^5-$, or $-C(R^5)_2-$, and R^5 is U_nR' ;

Q^2 and Q^3 are each independently a bond or a C_{1-6} alkylidene chain, wherein up to two methylene units of the chain are each optionally and independently replaced by $-S-$, $-O-$, $-CS-$, $-CO_2-$, $-OCO-$, $-CO-$, $-COCO-$, $-CONR'-$, $-NR'CO-$, $-NR'CO_2-$, $-SO_2NR'-$, $-NR'SO_2-$, $-CONR'NR'-$, $-NR'CONR'-$, $-OCONR'-$, $-NR'NR'-$, $-NR'SO_2NR'-$, $-SO-$, or $-SO_2-$, ~~$P(O)-$, $P(O)_2-$, or $P(OR')-$~~ ; and wherein any carbon atom in the one or more methylene units is optionally substituted with one or two occurrences of R^6 , wherein each occurrence of R^6 is independently halogen, CN , NO_2 , or U_nR' , or two occurrences of R^6 , or R' and R^6 , taken together with the atoms to which they are bound, form an optionally substituted 3-6-membered cycloalkyl, heterocyclyl, aryl or heteroaryl ring; [[and]]

~~Ar^1 and Ar^2 are each independently~~ is a 5-8 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from ~~nitrogen~~, oxygen[[,]] or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from ~~nitrogen~~, oxygen[[,]] or sulfur; wherein Ar^1 is and ~~Ar^2 are~~ each optionally substituted with 0-5 independent occurrences of TR^7 ; wherein T is a bond or is a C_1-C_6 alkylidene chain wherein up to two methylene units of T are optionally and

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independently replaced by -NR-, -S-, -O-, -CS-, -CO₂-, -OCO-, -CO-, -COCO-, -CONR-,
 -NRCO-, -NRCO₂-, -SO₂NR-, -NRSO₂-, -CONRNR-, -NRCONR-, -OCONR-, -NRNR-,
 -NRSO₂NR-, -SO-, or -SO₂-, ~~P(O)-, P(O)₂-, or P(OR')-~~;

Ar² is a 5-8 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein Ar² is optionally substituted with 0-5 independent occurrences of TR⁷; wherein T is a bond or is a C₁-C₆ alkylidene chain wherein up to two methylene units of T are optionally and independently replaced by -NR-, -S-, -O-, -CS-, -CO₂-, -OCO-, -CO-, -COCO-, -CONR-, -NRCO-, -NRCO₂-, -SO₂NR-, -NRSO₂-, -CONRNR-, -NRCONR-, -OCONR-, -NRNR-, -NRSO₂NR-, -SO-, or -SO₂-; and each occurrence of R⁷ is independently R', halogen, NO₂, or CN; or a pharmaceutically acceptable salt or composition thereof.

51. (Currently amended) The method of claim 50, comprising the additional step of administering to said patient an additional therapeutic agent selected from a chemotherapeutic or anti-proliferative agent selected from mechlorethamine, chlorambucil, cyclophosphamide, melphalan, ifosfamide, methotrexate, 6-mercaptopurine, 5-fluorouracil, cytarabine, gemcitabine, vinblastine, vincristine, vinorelbine, paclitaxel, etoposide, irinotecan, topotecan, doxorubicin, bleomycin, mitomycin, carmustine, lomustine, cisplatin, carboplatin, asparaginase, tamoxifen, leuprolide, flutamide, and megestrol, imatinib mesylate, adriamycin, dexamethasone, or cyclophosphamide; [[,]] an anti-inflammatory agent selected from albuterol or Singulair; ; an immunomodulatory or immunosuppressive agent, a neurotrophic factor, an anti-psychotic agent, or an agent for treating cardiovascular disease selected from a beta-blocker, an ACE inhibitors, a diuretic, a nitrate, a calcium channel blocker, or a statin, an

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~~agent for treating destructive bone disorders, an agent for treating liver disease, an anti-viral agent, an agent for treating blood disorders, an agent for treating diabetes, or an agent for treating immunodeficiency disorders, wherein:~~

said additional therapeutic agent is appropriate for the disease being treated; and

said additional therapeutic agent is administered together with said composition as a single dosage form or separately from said composition as part of a multiple dosage form.

52. (Previously presented) The method of claim 50, wherein said compound is used to treat or lessen the severity of breast cancer, colon cancer, kidney carcinoma, lung cancer, melanoma, ovarian cancer, pancreatic cancer, or prostate cancer.

53. (Currently amended) The method of claim 50, wherein said compound is used to treat or lessen the severity of ~~cardiomegaly~~, hypertension, angina pectoris, ~~cerebrovascular contraction, cerebral vasospasm, coronary vasospasm, myocardial hypertrophy~~, ischemia/reperfusion-induced injury, ~~endothelial dysfunction~~, or erectile dysfunction.

54. (Previously presented) The method of claim 50, wherein said compound is used to treat or lessen the severity of Alzheimer's disease.

55. (Previously presented) The method of claim 50, wherein said compound is used to treat or lessen the severity of an allergy or asthma.

56. (Previously presented) The method of claim 50, wherein said compound is used to treat or lessen the severity of diabetes.